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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Sep 17	IMSworld Pharmaceutical Company Directory name change to PHARMASEARCH
NEWS 3	Oct 09	Korean abstracts now included in Derwent World Patents Index
NEWS 4	Oct 09	Number of Derwent World Patents Index updates increased
NEWS 5	Oct 15	Calculated properties now in the REGISTRY/ZREGISTRY File
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NEWS 7	Oct 22	DGENE GETSIM has been improved
NEWS 8	Oct 29	AAASD no longer available
NEWS 9	Nov 19	New Search Capabilities USPATFULL and USPAT2
NEWS 10	Nov 19	TOXCENTER(SM) - new toxicology file now available on STN
NEWS 11	Nov 29	COPPERLIT now available on STN
NEWS 12	Nov 29	DWPI revisions to NTIS and US Provisional Numbers
NEWS 13	Nov 30	Files VETU and VETB to have open access
NEWS 14	Dec 10	WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS 15	Dec 10	DGENE BLAST Homology Search
NEWS 16	Dec 17	WELDASEARCH now available on STN
NEWS 17	Dec 17	STANDARDS now available on STN
NEWS 18	Dec 17	New fields for DPCI
NEWS 19	Dec 19	CAS Roles modified
NEWS 20	Dec 19	1907-1946 data and page images added to CA and CAplus
NEWS 21	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 22	Jan 25	Searching with the P indicator for Preparations
NEWS 23	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 24	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 25	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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L5 ANSWER 1 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
1999:415247 Document No.: PREV199900415247. Role of disulfide bonds upon the structural stability of an amaranth globulin. Castellani, Oscar F. (1); Martinez, E. Nora; Anon, M. Cristina (1). (1) Centro de Investigacion y Desarrollo en Criotecnologia de Alimentos (CIDCA), Facultad de Ciencias Exactas, Consejo Nacional de Investigaciones Cientificas y Tecnicas (CONICET), Universidad Nacional de La Plata (UNLP), 47 y 116 (1900), La Plata Argentina. Journal of Agricultural and Food Chemistry, (Aug., 1999) Vol. 47, No. 8, pp. 3001-3008. ISSN: 0021-8561. Language: English. Summary Language: English.

AB Analysis of globulin-P, the polymerized amaranth globulin, gave a low amount of free sulfhydryls (10.2 +- 0.5 mumol/g) from which 7 +- 1 mumol/g was buried inside the molecule. In addition, its disulfide content was high (51 +- 1 mumol/g) and similar to soybean 11S globulin content. The more exposed disulfide bridges were found to be stabilizing polymers, whereas the less reactive bridges were either linking P20 and **P30 polypeptides** or forming intrachain linkages. It was found that the buried bonds participate in the stabilization of folded polypeptides and the quaternary structure of the globulin. In turn, the dissociation of

polymers and disruption of the quaternary structure by the action of 2-mercaptoethanol reverted upon removal of the reducing agent. This demonstrates that the polymerized state and the quaternary structure of the molecules are most favorable from the thermodynamic point of view. The similar content of SH and SS in globulin-P and globulin-S found in this laboratory suggests that the differences between these proteins may be ascribed to other compositional differences.

L5 ANSWER 2 OF 21 SCISEARCH COPYRIGHT 2002 ISI (R)
91:339851 The Genuine Article (R) Number: FP296. IMMUNOGOLD LOCALIZATION OF A NOVEL ADHESIVE MOLECULE, AMPHOTERIN (P-30) IN ROTARY-SHADOWED HUMAN FIBROBLASTS. WARTIOVAARA J J (Reprint); PIHLASKARI R; RAUVALA H. UNIV HELSINKI, DEPT ELECTRON MICROSCOPY, MANNERHEIMINTIE 172, SF-00300 HELSINKI, FINLAND (Reprint); UNIV HELSINKI, DEPT MED CHEM, SF-00300 HELSINKI, FINLAND. INSTITUTE OF PHYSICS CONFERENCE SERIES (1990) No. 98, pp. 685-686. Pub. country: FINLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The novel **p30-polypeptide** amphoterin, previously described in perinatal rat brain neurons and neuroblastoma cells was shown to be expressed also in human fibroblasts. The protein, suggested to have adhesive function in neurite growth, was localized also in spreading fibroblasts especially to filopodial cell extensions as seen in monolayer cells by immunofluorescence and by immunogold labeling followed by rotary-shadowing.

L5 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2002 ACS
1991:204187 Document No. 114:204187 Immunogold localization of a novel adhesive molecule, amphoterin (p30) in rotary-shadowed human fibroblasts. Wartiovaara, J. J.; Pihlaskari, R.; Rauvala, H. (Dep. Electron Microsc., Univ. Helsinki, Helsinki, 00300, Finland). Inst. Phys. Conf. Ser., 98(EMAG-MICRO 89, Vol. 2), 685-6 (English) 1990. CODEN: IPCSEP. ISSN: 0951-3248.
AB The novel **p30-polypeptide**, amphoterin, previously described in perinatal rat brain neurons and neuroblastoma cells, was shown to be expressed also in human fibroblasts. The protein, suggested to have adhesive function in neurite growth, was localized also in spreading fibroblasts esp. in filopodial cell extensions, as seen in monolayer cells by immunofluorescence and by immunogold labeling followed by rotary-shadowing.

L5 ANSWER 4 OF 21 MEDLINE DUPLICATE 2
89174601 Document Number: 89174601. PubMed ID: 2925621. The major surface antigen, P30, of Toxoplasma gondii is anchored by a glycolipid. Nagel S D; Boothroyd J C. (Department of Microbiology and Immunology, Stanford University School of Medicine, California 94305.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1989 Apr 5) 264 (10) 5569-74. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.
AB P30, the major surface antigen of the parasitic protozoan Toxoplasma gondii, can be specifically labeled with [3H]palmitic acid and with myo-[2-3H]inositol. The fatty acid label can be released by treatment of P30 with phosphatidylinositol-specific phospholipase C (PI-PLC). Such treatment exposes an immunological "cross-reacting determinant" first described on Trypanosoma brucei variant surface glycoprotein. PI-PLC cleavage of intact parasites metabolically labeled with [35S]methionine results in the release of intact **P30 polypeptide** in a form which migrates faster in polyacrylamide gel electrophoresis. These results argue that P30 is anchored by a glycolipid. Results from thin layer chromatography analysis of purified [3H] palmitate-labeled P30 treated with PI-PLC, together with susceptibility to mild alkali hydrolysis and to cleavage with phospholipase A2, suggest that the glycolipid anchor of T. gondii P30 includes a 1,2-diacylglycerol moiety.

L5 ANSWER 5 OF 21 MEDLINE DUPLICATE 3
87096151 Document Number: 87096151. PubMed ID: 2432739. Antigenic

differences among multiply charged Moloney murine leukemia virus **p30 polypeptides** found inside infected cells. Ikuta K; Luftig R B. VIRUS RESEARCH, (1986 Nov) 6 (2) 101-8. Journal code: X98; 8410979. ISSN: 0168-1702. Pub. country: Netherlands. Language: English.

AB At least three Moloney murine leukemia virus (M-MuLV) **p30 polypeptides** (p30's), viz., a major species at pI 6.3 and two minor ones at pI 6.1 and pI 6.6, have previously been identified in purified virions by 2-dimensional gel electrophoresis and chromatofocusing (Katoh, I., Yoshinaka, Y. and Luftig, R.B. (1984) J. Gen. Virol. 65, 733-741). We have observed a similar, but distinctive pI pattern for [35S]methionine-labeled MuLV p30's in lysates from chronically infected (MuLV) cells. The variation in pI pattern of the intracellular MuLV p30's was dependent on the type of p30 reactive antibody used for immunoprecipitation. Specifically: a p30 spot with pI 6.3 was always precipitated as the major spot with three different antibodies, minor spots with pI 6.0 and 6.6 were variably seen dependent on the antibody used, and an intracellular p30 spot at pI 6.1 was only precipitated with a rat p30 monoclonal antibody but not with monospecific mouse or intact MuLV cross-reacting p30 sera. These results indicate that first, there are differences between the pI pattern of virion and intracellular MuLV p30's, and second, the antigenic determinants of intracellular p30's vary dependent on the antibody used for immunoprecipitation.

L5 ANSWER 6 OF 21 MEDLINE DUPLICATE 4

86238283 Document Number: 86238283. PubMed ID: 3915177. Differential translation of virogenic and oncogenic sequences in malignant lymphoproliferative diseases and transfection of coding DNAs into NIH 3T3 cells. Toth F D; Vaczi L; Szabo B; Kiss J; Rak K; Kiss A; Kovacs I; Kiss C; Pecze K. ACTA MICROBIOLOGICA HUNGARICA, (1985) 32 (4) 341-50. Journal code: 1AH; 8400270. ISSN: 0231-4622. Pub. country: Hungary. Language: English.

AB The expression of oncoviral **p30 polypeptides** and onc gene-specific proteins has been examined in different human lymphoid malignancies. The distribution of antigen(s) related to the p30 of BaEV lacked any specificity. Antigen(s) related to the main core polypeptide of GaLV could be detected mainly in B- and O-cell malignancies. The myc-encoded protein was translated at higher levels in malignant than in normal lymphoid cells. An active src gene was identified in three acute lymphoid leukaemias and in one non-Hodgkin lymphoma of T-cell origin. Human DNAs coding oncoviral antigens or onc gene-specific proteins could be transfected into NIH 3T3 cells. These data suggest that the synergistic effect of the myc and src genes would operate in malignant transformation of some progenitors of T-cell lineage.

L5 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2002 ACS

1986:106100 Document No. 104:106100 Differential translation of virogenic and oncogenic sequences in malignant lymphoproliferative diseases and transfection of coding DNAs into NIH 3T3 cells. Toth, F. D.; Vaczi, L.; Szabo, B.; Kiss, Jolan; Rak, K.; Kiss, A.; Kovacs, Ilona; Kiss, C.; Pecze, K. (Inst. Microbiol., Univ. Med. Sch., Debrecen, Hung.). Acta Microbiol. Hung., 32(4), 339-48 (English) 1985. CODEN: AMHUEF.

AB The expression of oncoviral **p30 polypeptides** and onc gene-specific proteins was examd. in different human lymphoid malignancies. The distribution of antigen(s) related to the p30 of baboon endogenous virus lacked any specificity. Antigen(s) related to the main core polypeptide of gibbon ape leukemia virus could be detected mainly in B- and O-cell malignancies. The myc-encoded protein was translated at higher levels in malignant than in normal lymphoid cells. An active src gene was identified in 3 acute lymphoid leukemias and in 1 non-Hodgkin lymphoma of T-cell origin. Human DNAs coding oncoviral antigens or onc gene-specific proteins could be transfected into NIH 3T3 cells. These data suggest that the synergistic effect of the myc and src genes would operate in malignant transformation of some progenitors of T-cell lineage.

L5 ANSWER 8 OF 21 MEDLINE DUPLICATE 5
82132415 Document Number: 82132415. PubMed ID: 6120639. Detection by radioimmunoassay of antigens related to the **P30 polypeptides** of primate type C oncoviruses in peripheral leukocytes from patients with chronic myelogenous leukaemia. Toth F D; Vaczi L; Kiss J; Rethy A; Kiss A; Rak K. ACTA VIROLOGICA, (1981 Nov) 25 (6) 376-80. Journal code: 286; 0370401. ISSN: 0001-723X. Pub. country: Czechoslovakia. Language: English.

AB Leukocytes from patients with chronic myelogenous leukaemia were examined for antigens related to the **p30 polypeptides** of baboon endogenous virus (BaEV) and gibbon ape leukaemia virus (GaLV). Samples from patients with the quiescent phase of the disease proved to be negative or contained p30 of BaEV as the only viral antigen. In cases of blastoid crisis or acceleration, an antigen related to p30 of GaLV could be detected. In 5 of 6 patients, acceleration or blastoid crisis was preceded by expression of GaLV p30.

L5 ANSWER 9 OF 21 MEDLINE DUPLICATE 6
81193616 Document Number: 81193616. PubMed ID: 7229618. Analysis of the origin of charge heterogeneity of Rauscher murine leukaemia virus p30. Brouwer J; Warnaar S O. JOURNAL OF GENERAL VIROLOGY, (1980 Dec) 51 (Pt 2) 409-14. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Preparations of the 30 X 10(3) mol. wt. protein (p30) of Rauscher murine leukaemia virus (R-MuLV) which had been purified to homogeneity as judged by gel electrophoresis in the presence of SDS and by amino-terminal amino acid analysis, showed considerable isoelectric heterogeneity. It was found that R-MuLV **p30 polypeptide** chains are easily converted in vitro into chains with more acidic isoelectric points. R-MuLV **p30 polypeptides** with different isoelectric points displayed the same set of 125I-labelled tryptic peptides. It is concluded that the charge heterogeneity of R-MuLV p30, as revealed in isoelectric focusing experiments, is not caused by genetic heterogeneity of the virus genome but by post-translational modification.

L5 ANSWER 10 OF 21 MEDLINE
80136714 Document Number: 80136714. PubMed ID: 6244236. Detection of B-tropic endogenous type-C virus in viral isolates originating from induced BALB/K-3T3 cells. Laprevotte I; Chuat J C; Pilon C. INTERVIROLOGY, (1980) 12 (6) 316-28. Journal code: GW7; 0364265. ISSN: 0300-5526. Pub. country: Switzerland. Language: English.

AB Isoelectric focusing (IEF) analysis of class I endogenous type-C virus induced by iododeoxyuridine treatment of BALB/K-3T3 cells revealed, in addition to the major variant of the **p30 polypeptide**, which has an isoelectric point of 6.1 (pI 6.1 isop30), a minor isop30 with a pI of 5.6. This value was also found for a prototype BALB/c B-tropic endogenous virus isolate. The pI 5.6 isop30 of the N-tropic isolate was amplified by long-term virus replication in B-type mouse cells, and comparative IEF and XC-assay data suggest that it may correspond to a B-tropic subpopulation which has not yet been detected in vitro in mouse cells of embryonic origin.

L5 ANSWER 11 OF 21 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 7
81002741 EMBASE Document No.: 1981002741. Pathogenesis of the slow disease of the central nervous system associated with wild mouse virus: II. Role of virus and host gene products. Oldstone M.B.A.; Jensen F.; Dixon F.J.; Lampert P.W.. Dept. Immunopathol., Scripps Clin. Res. Found., La Jolla, Calif. 92037, United States. Virology 107/1 (180-193) 1980. CODEN: VIRLAX. Pub. Country: United States. Language: English.

AB Several wild mouse viruses cause a slow disease of the central nervous system (CNS) that is marked by injury in neurons predominantly in the anterior horn of the spinal cord, dentate nucleus of the cerebellum, and the brain stem. This injury is translated into a progressive paralytic illness. Also, injury of oligodendrocytes occurs which leads to primary

demyelination, all in the absence of an inflammatory response. After exposure to high titers of virus, inbred mice of separate strains differ dramatically in their incidence of the associated CNS disease. To sort out the factors of the viruses themselves, as well as the host's genetic loci that affect and thereby control the interaction of virus with host, we have studied various inbred and recombinant mouse strains as well as wild mouse viruses that differ structurally from each other by ENV or GAG gene products. We find that both the major ENV (gp 69/70) and the major GAG (p30) gene products are necessary to cause disease. After the entry of virus into susceptible cells, a **p30 polypeptide**(s) coded for by the GAG gene accumulates in CNS tissues and closely parallels the severity of the disease. Disease manifestation appears to be controlled by two recessive genes of the host and is associated with the FV-1n host gene locus or a closely related area, but not the major histocompatibility complex transplantation antigens.

L5 ANSWER 12 OF 21 MEDLINE DUPLICATE 8
79131734 Document Number: 79131734. PubMed ID: 422956. Chemical characterization of Rauscher leukaemia virus proteins. Brouwer J; Pluijms W J; Warnaar S O. JOURNAL OF GENERAL VIROLOGY, (1979 Feb) 42 (2) 415-21. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The proteins of Rauscher murine leukaemia virus (R-MuLV) were characterized by amino acid analyses and by determination of their mol. wt. by gel filtration on cross-linked Sepharose 6B in 6M-guanidine hydrochloride (GuHCl). Molecular weights of 56,000, 29,000, 15,000, 10,500 and 7,600 were found for gp70, p30, p15, p12 and p10 respectively. The amino acid compositions of these proteins and of p12E have been determined. The amino acid compositions of the p10 polypeptides of Rauscher-MuLV and Moloney-MuLV are very similar as are those of the **p30 polypeptides**, whereas the amino acid compositions of the p12 polypeptides differ considerably. P12E contains the highest percentage of hydrophobic amino acid residues. Among the gag-gene coded proteins, p15 contains the highest percentage of hydrophobic amino acid residues while p12 and p10 contain the lowest.

L5 ANSWER 13 OF 21 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 9
80075396 EMBASE Document No.: 1980075396. Detection of B-tropic endogenous type-C virus in viral isolates originating from induced BALB/K-3T3 cells. Laprevotte I.; Chuat J.C.; Pilon C.. Dept. Oncol. Exp., Inst. Rech. Mal. Sang, Hop. St Louis, Paris, France. Intervirology 12/6 (316-328) 1979. CODEN: IVRYAK. Pub. Country: Switzerland. Language: English.

AB Isoelectric focusing (IEF) analysis of class I endogenous type-C virus induced by iododeoxyuridine treatment of BALB/K-3T3 cells revealed, in addition to the major variant of the **p30 polypeptide**, which has an isoelectric point of 6.1 (pI 6.1 isop30), a minor isop30 with a pI of 5.6. This value was also found for a prototype BALB/c B-tropic endogenous virus isolate. The pI 5.6 isop30 of the N-tropic isolate was amplified by long-term virus replication in B-type mouse cells, and comparative IEF and XC-assay data suggest that it may correspond to a B-tropic subpopulation which has not yet been detected in vitro in mouse cells of embryonic origin.

L5 ANSWER 14 OF 21 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1979:259350 Document No.: BA68:61854. EXPRESSION OF ONCORNAVIRUS ANTIGENS IN PERIPHERAL LEUKOCYTES OF PATIENTS WITH CHRONIC MYELOID LEUKEMIA. TOTH F D; MADAR Z; KISS J; JAKO J; VACZI L; RAK K. INST. MICROBIOL., UNIV. MED. SCH., P.O. BOX 17, H-4012 DEBRECEN, HUNG.. ACTA MICROBIOL ACAD SCI HUNG, (1979) 26 (1), 47-54. CODEN: AMAHA5. ISSN: 0001-6187. Language: English.

AB Peripheral leukocytes from 16 patients with chronic myeloid leukemia (CML) were examined for the presence of oncornavirus **p30** [**polypeptide**] antigens by indirect cytoplasmic immunofluorescence. The leukocytes of 12 patients who could be kept in balance by chemotherapy proved negative or contained the p30 antigen of mammalian endogenous

oncornaviruses as the only viral antigen. In the leukocytes of 4 patients being in blastoid crisis, an antigen related to the p30 antigen of mammalian leukemia-sarcoma viruses was detected. In 5 of 6 patients decrease in sensitivity to chemotherapy, or blastoid crisis, was preceded by expression of leukemia-sarcoma virus p30 antigen(s). Leukocytes from 15 CML patients kept in balance by chemotherapy and those from 7 being in blastoid crisis were examined by indirect membrane immunofluorescence for the presence of antigen(s) related to the gp70 [glycoprotein] antigen of the simian and murine leukemia-sarcoma virus. All tests proved negative.

L5 ANSWER 15 OF 21 MEDLINE DUPLICATE 10
78088613 Document Number: 78088613. PubMed ID: 202669. The isoelectric point of the **p30 polypeptide** as a marker of mouse endogenous viruses. Chuat J C; Laprevotte I; Bernard C; Pilon C. JOURNAL OF GENERAL VIROLOGY, (1978 Jan) 38 (1) 169-73. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The isoelectric point (PI) of the **p30 polypeptide** of members of the three known classes of mouse C-type endogenous viruses was determined both by column and by thin-layer gel isoelectric focusing. Each class was found to be characterized by a particular variant of p30 (isop30), with pI values of 6.1 for class I (ecotropic), 5.7 for class II (xenotropic), and 5.5 for class III (NZB, NIH, ATS124, also xenotropic). The 6.1-isop30 was found as a minor component of rat-grown NZB virus and of a number of laboratory strains of mouse C-type viruses.

L5 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2002 ACS
1977:435545 Document No. 87:35545 Induction of murine C-type endogenous viruses. Attempt at discrimination based on the isoelectric point of the **p30 polypeptide** and on the pattern of cellular transformation. Laprevotte, Ivan; Chuat, Jean Claude; Bernard, Carmen; Canivet, Martine; Pilon, Catherine (Lab. Hematol. Exp., Hop. Saint-Louis, Paris, Fr.). C. R. Hebd. Seances Acad. Sci., Ser. D, 284(17), 1737-40 (French) 1977. CODEN: CHDDAT.

AB Endogenous ecotropic and xenotropic murine C-type viruses induced in K-Balb-3T3 cells treated with iododeoxyuridine were selected by infection of appropriate indicator cells. The isoelec. point (pI) of the major viral polypeptide (p30) was 6.1 for the ecotropic virus (class I), and 5.7 for the xenotropic virus (class II). An isoelec. form (iso p30) of pI 6.5 was obsd. in the initial induction peak. In addn., the pattern of cellular alteration in NRK cells at its onset varied according to the pseudotype, the class I pseudotype inducing round cell foci while the foci assocd. with the class II pseudotype consisted of fusiform cells.

L5 ANSWER 17 OF 21 MEDLINE DUPLICATE 11
77114124 Document Number: 77114124. PubMed ID: 65230. Cells transformed by certain strains of Moloney sarcoma virus contain murine p60. Robey W G; Oskarsson M K; Woude G F; Naso R B; Arlinghaus R B; Haapala D K; Fischinger P J. CELL, (1977 Jan) 10 (1) 79-89. Journal code: CQ4; 0413066. ISSN: 0092-8674. Pub. country: ENGLAND: United Kingdom. Language: English.

AB It was previously demonstrated that the 60,000 dalton (p60) precursor-like polyprotein containing murine p30 was a constituent of the feline leukemia virus pseudotype of Moloney sarcoma virus [m1MSV(FeLV)]. It is now shown that p60 is detected in cells of five mammalian species transformed by m1MSV, indicating that p60 is specified by this genome. Moreover, little or no murine p30 is detected in the m1MSV-transformed cells, suggesting that the murine group p30 antigenic reactivity of S + L- cells is ude to p60. Pulse-chase studies in cells producing m1MSV(FeLV) show that p60 is the largest polypeptide detectable during the pulse, and that intracellular p60 is not cleaved into smaller (for example, **p30**) **polypeptides** during chase periods of up to 10 hr. The lack of cleavage of p60 is in contrast to the properties of p30 precursors detected in cells containing replicating avian or mammalian RNA tumor

viruses. The inefficient cleavage of intracellular p60 and the kinetics of appearance of murine p30 in extracellular m1MSV(FeLV) suggest that p60 cleavage to p30 occurs in cells shortly before virus release. While only p60 was detected in the m1MSV-transformed cells, p60 and p70 were detected in m3MSV-transformed cells, and no immunoprecipitable polypeptides were detected in HT-1 MSV-transformed cells. The observed differences in the intracellular polypeptide expression by each of the strains of MSV suggests differences in genetic content.

L5 ANSWER 18 OF 21 MEDLINE DUPLICATE 12
77074297 Document Number: 77074297. PubMed ID: 63563. Detection, quantitation, and characterization of the major internal virion antigen of the bovine leukemia virus by radioimmunoassay. McDonald H C; Ferrer J F. JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1976 Oct) 57 (4) 875-82. Journal code: J9J; 7503089. ISSN: 0027-8874. Pub. country: United States. Language: English.

AB The major internal polypeptide of the bovine leukemia virus (BLV) was purified to homogeneity with the use of gel filtration and affinity chromatography. Like previous results, the protein had a molecular weight of 25,000 daltons as determined by electrophoresis in polyacrylamide gels with sodium dodecyl sulfate. More than 90% of the 125I-labeled protein was precipitated by bovine sera that reacted in immunofluorescence tests with acetone-fixed BLV-infected cells. In contrast, minimal precipitation (less than 5%) was observed with sera from 36 cattle in leukemia-free herds; these sera, negative by immunofluorescence, included six samples that had high titers of antibodies to the foamy-like bovine syncytia virus (BSV). Antisera prepared against several other oncornaviruses or the Mason-Pfizer monkey virus (M-PMV) did not bind the BLV p25 protein. Conversely, the labeled **p30 polypeptides** of several oncornaviruses tested did not react with bovine sera that had high titers of antibodies to BLV p25. Competitive radioimmunoassay(s) (RIA) also failed to detect cross-reactions between BLV p25 protein and the internal polypeptides of other mammalian and avian oncornaviruses, M-PMV, or foamy-like BSV. The RIA for BLV p25 antigen was also highly sensitive and specific for the detection and quantitation of the antigen in virus preparations and cell homogenates.

L5 ANSWER 19 OF 21 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
77212421 EMBASE Document No.: 1977212421. Detection, quantitation, and characterization ofthe major internal virion antigen of the bovine leukemia virus by radioimmunoassay. McDonald Ferrer H.C.J.F.. Univ. Pennsylvania Sch. Veter. Med., New Bolton Cent., Pa. 19348, United States. Journal of the National Cancer Institute 57/4 (875-882) 1976. CODEN: JNCIAM. Language: English.

AB The major internal polypeptide of the bovine leukemia virus (BLV) was purified to homogeneity with the use of gel filtration and affinity chromatography. Like previous results, the protein had a molecular weight of 25,000 daltons as determined by electrophoresis in polyacrylamide gels with sodium dodecyl sulfate. More than 90% of the 125I labeled protein was precipitated by bovine sera that reacted in immunofluorescence tests with acetone fixed BLV infected cells. In contrast, minimal precipitation (<5%) was observed with sera from 36 cattle in leukemia free herds; these sera, negative by immunofluorescence, included six samples that had high titers of antibodies to the foamy like bovine syncytia virus (BSV). Antisera prepared against several other oncornaviruses or the Mason Pfizer monkey virus (M PMV) did not bind the BLV p25 protein. Conversely, the labeled **p30 polypeptides** of several oncornaviruses tested did not react with bovine sera that had high titers of antibodies to BLV p25. Competitive radioimmunoassay(s) (RIA) also failed to detect cross reactions between BLV p25 protein and the internal polypeptides of other mammalian and avian oncornaviruses, M PMV, or foamy like BSV. The RIA for BLV p25 antigen was also highly sensitive and specific for the detection and quantitation of the antigen in virus preparations and cell homogenates.

L5 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2002 ACS
1976:14452 Document No. 84:14452 Isoelectric point variants of the major polypeptide (p 30) in murine oncornavirus stocks. Chuat, Jean C.; Laprevotte, Ivan; Boiron, Michel (Inst. Rech. Leucemies Mal. Sang, Hop. Saint-Louis, Paris, Fr.). C. R. Hebd. Seances Acad. Sci., Ser. D, 281(14), 1051-4 (French) 1975. CODEN: CHDDAT.
AB Murine oncornavirus polypeptide p30 exists in different forms which are separable by electrofocusing and have isoelectric points (pIs) of 5.5, 5.9, 6.7, and 7.1. A pI of 5.9 is characteristic of the peptide from Moloney virus. The viral stocks of other strains include 3-4 differently charged **p30 polypeptides**, with a predominance of the pI 6.7 species in Gross strains.

L5 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2002 ACS
1975:84155 Document No. 82:84155 Expression of murine leukemia virus structural antigens on the surface of chemically induced murine sarcomas. Grant, John P.; Bigner, Darell D.; Fischinger, Peter J.; Bolognesi, Dani P. (Med. Cent., Duke Univ., Durham, N. C., USA). Proc. Natl. Acad. Sci. U. S. A., 71(12), 5037-41 (English) 1974. CODEN: PNASA6.
AB Cultured cells of different chem. induced C57BL/6N murine sarcomas produced variable amts. of infectious murine leukemia virus (MuLV) and contained proportional amts. of MuLV structural components as detd. by radioimmunoassay. Monospecific antiserums directed against the major MuLV glycoprotein (gp71), the major internal antigen (p30), and the ribonucleoprotein (p10) were capable of mediating tumor cell lysis in the presence of complement, suggesting that these viral structural components were localized at least in part to the cell surface. Membrane immunofluorescence studies with MuLV p30 antiserum confirmed surface localization. Addn. of MuLV **p30 polypeptide** to normal cells and tumor cells enhanced the cytotoxicity of MuLV p30 antiserum. Apparently the presence of MuLV structural components, on cell surfaces can be independent of virus prodn. and cellular transformation.

=> s "HVEM" polypeptide
L6 2 "HVEM" POLYPEPTIDE

=> dup remove l6
PROCESSING COMPLETED FOR L6
L7 2 DUP REMOVE L6 (0 DUPLICATES REMOVED)

=> d l7 1-2 cbib abs

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
2001:781125 Document No. 135:343309 Ligand p30/LIGHT for HVEM (herpes virus entry mediator) and methods of therapeutic use. Ware, Carl F. (La Jolla Institute for Allergy and Immunology, USA). PCT Int. Appl. WO 2001079496 A2 20011025, 104 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US11857 20010411. PRIORITY: US 2000-524325 20000313; US 2000-549096 20000412.
AB A novel polypeptide ligand, p30, for HVEM (herpes virus entry mediator) and functional variations and fragments thereof are provided. The HVEM ligand is isolated from II-23.D7 cell line, a human CD4+ T cell hybridoma. P30, which can be found as a membrane protein and can function as a cytokine, is also called LIGHT, because this polypeptide is homologous to Lymphotoxins, exhibits Inducible expression, and competes with HSV

Glycoprotein D for HVEM, a receptor expressed by T lymphocytes. Because LIGHT can compete with HSV glycoprotein D for HVEM, homo-trimeric sol. forms of this polypeptide can be used to block the entry of herpesvirus into cells. P30 is useful for modulating immune responses and in inhibiting infection and/or subsequent proliferation by herpesvirus. LIGHT also bind to the lymphotoxin-.beta. receptor (LT.beta.R). The present invention is also based upon the discovery that **HVEM polypeptides** have an antagonistic effect on inflammation. In particular, HVEM fusion proteins are capable of inhibiting inflammation when administered to a subject. HVEM-Fc fusion proteins are also provided. Methods for treating subjects with lymphoid cell disorders, tumors, autoimmune diseases, inflammatory disorders of those having or suspected of having a herpes virus infection, utilizing p30 and the fusion proteins of the invention, are also provided.

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
1998:405987 Document No. 129:94450 Herpesvirus entry mediator (**HVEM**) **polypeptides** and uses thereof. Ashkenazi, Avi J.; Marsters, Scot A. (Genentech, Inc., USA). PCT Int. Appl. WO 9825967 A1 19980618, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US22278 19971205. PRIORITY: US 1996-32705 19961212.
AB Novel polypeptides, designated HVEM, are provided. Compns. including HVEM chimeras, nucleic acid encoding HVEM, and antibodies to HVEM are also provided. Also claimed were non-human transgenic animal or knockout mice or rats that expressing **HVEM polypeptide** or altered HVEM gene and polypeptide. The HVEM protein, gene, antibody, chimeras, are transgenic animal are useful in understanding HVEM protein in pathol. condition and in therapy and nontherapy applications. The nucleic acid sequence and amino acid sequence of HVEM were detd. and are similar to human tumor necrosis factor receptor family.

```
=> s lymphotoxin beta receptor
L8          516 LYMPHOTOXIN BETA RECEPTOR

=> s l8 and soluble
L9           71 L8 AND SOLUBLE

=> s l9 and T cell proliferation
   2 FILES SEARCHED...
L10           5 L9 AND T CELL PROLIFERATION

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L11            2 DUP REMOVE L10 (3 DUPLICATES REMOVED)

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L11 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2001:265922 Document No.: PREV200100265922. TNFRSF19L, a new member of tumor necrosis factor receptor superfamily, that is expressed in lymphoid organs and activates NF-kappaB. Sica, Gabriel (1); Zhu, Gefeng (1); Tamada, Koji (1); Liu, Ding; Ni, Jian; Chen, Lieping (1). (1) Mayo Clinic, 200 1st Street SW, Rochester, MN, 55905 USA. FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A700. print. Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001 ISSN: 0892-6638. Language: English. Summary Language: English.

AB We have cloned a new member of the TNFR superfamily, TNFRSF19L (Tumor Necrosis Factor Receptor Superfamily 19 Like). TNFRSF19L is a type I transmembrane glycoprotein with a cysteine rich extracellular domain that shares significant homology to TNFRSF19, decoy receptor 3, OX40, and **lymphotoxin beta receptor**. The mRNA of TNFRSF19L is especially abundant in lymphoid organs such as spleen, lymph node, and peripheral blood leukocytes as well as in leukemias and lymphomas. Overexpression of TNFRSF19L in 293 cells leads to the activation of the NF-kappaB pathway that is independent of TRAF 1, 2, 3, 5 and 6 binding. While the **soluble** form of TNFRSF19L fusion protein does not inhibit the one way mixed lymphocyte reaction, immobilized TNFRSF19L is capable of costimulating **T cell proliferation** in the presence of CD3 signaling. Our results define a new member of the TNFR superfamily that may be a potential regulator for immune responses.

L11 ANSWER 2 OF 2 MEDLINE DUPLICATE 1
2000219245 Document Number: 20219245. PubMed ID: 10754304. LIGHT, a TNF-like molecule, costimulates **T cell proliferation** and is required for dendritic cell-mediated allogeneic T cell response. Tamada K; Shimozaki K; Chapoval A I; Zhai Y; Su J; Chen S F; Hsieh S L; Nagata S; Ni J; Chen L. (Department of Immunology, Mayo Graduate and Medical Schools, Mayo Clinic, Rochester, MN 55905, USA.) JOURNAL OF IMMUNOLOGY, (2000 Apr 15) 164 (8) 4105-10. Journal code: IFB; 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB LIGHT is a recently identified member of the TNF superfamily and its receptors, herpesvirus entry mediator and **lymphotoxin beta receptor**, are found in T cells and stromal cells. In this study, we demonstrate that LIGHT is selectively expressed on immature dendritic cells (DCs) generated from human PBMCs. In contrast, LIGHT is not detectable in DCs either freshly isolated from PBMCs or rendered mature in vitro by LPS treatment. Blockade of LIGHT by its **soluble** receptors, **lymphotoxin beta receptor**-Ig or HVEM-Ig, inhibits the induction of DC-mediated primary allogeneic T cell response. Furthermore, engagement of LIGHT costimulates human **T cell proliferation**, amplifies the NF-kappaB signaling pathway, and preferentially induces the production of IFN-gamma, but not IL-4, in the presence of an antigenic signal. Our results suggest that LIGHT is a costimulatory molecule involved in DC-mediated cellular immune responses.

```
=> s "gD"
L12     283726 "GD"

=> s l12 and polypeptide
L13       3312 L12 AND POLYPEPTIDE

=> s l13 and HSV-1
L14        164 L13 AND HSV-1

=> s l14 and mutant
L15         47 L14 AND MUTANT

=> s l15 and cell proliferation
   3 FILES SEARCHED...
L16          0 L15 AND CELL PROLIFERATION

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L17          32 DUP REMOVE L15 (15 DUPLICATES REMOVED)

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L17 ANSWER 1 OF 32 MEDLINE
1999292852 Document Number: 99292852. PubMed ID: 10364308. ICP22 and the UL13 protein kinase are both required for herpes simplex virus-induced modification of the large subunit of RNA polymerase II. Long M C; Leong V; Schaffer P A; Spencer C A; Rice S A. (Departments of Biochemistry, University of Alberta, Edmonton, Alberta, Canada T6G 2H7.) JOURNAL OF VIROLOGY, (1999 Jul) 73 (7) 5593-604. Journal code: KCV; 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Herpes simplex virus type 1 (**HSV-1**) infection alters the phosphorylation of the large subunit of RNA polymerase II (RNAP II), resulting in the depletion of the hypophosphorylated and hyperphosphorylated forms of this **polypeptide** (known as IIa and IIo, respectively) and induction of a novel, alternatively phosphorylated form (designated IIi). We previously showed that the **HSV-1** immediate-early protein ICP22 is involved in this phenomenon, since induction of IIi and depletion of IIa are deficient in cells infected with 22/n199, an **HSV-1** ICP22 nonsense **mutant** (S. A. Rice, M. C. Long, V. Lam, P. A. Schaffer, and C. A. Spencer, J. Virol. 69:5550-5559, 1995). However, depletion of IIo still occurs in 22/n199-infected cells. This suggests either that another viral gene product affects the RNAP II large subunit or that the truncated ICP22 **polypeptide** encoded by 22/n199 retains residual activity which leads to IIo depletion. To distinguish between these possibilities, we engineered an **HSV-1** ICP22 null **mutant**, d22-lacZ, and compared it to 22/n199. The two **mutants** are indistinguishable in their effects on the RNAP II large subunit, suggesting that an additional viral gene product is involved in altering RNAP II. Two candidates are UL13, a protein kinase which has been implicated in ICP22 phosphorylation, and the virion host shutoff (Vhs) factor, the expression of which is positively regulated by ICP22 and UL13. To test whether UL13 is involved, a UL13-deficient viral **mutant**, d13-lacZ, was engineered. This **mutant** was defective in IIi induction and IIa depletion, displaying a phenotype very similar to that of d22-lacZ. In contrast, a Vhs **mutant** had effects that were indistinguishable from wild-type **HSV-1**. Therefore, UL13 but not the Vhs function plays a role in modifying the RNAP II large subunit. To study the potential role of UL13 in viral transcription, we carried out nuclear run-on transcription analyses in infected human embryonic lung cells. Infections with either UL13 or ICP22 **mutants** led to significantly reduced amounts of viral genome transcription at late times after infection. Together, our results suggest that ICP22 and UL13 are involved in a common pathway that alters RNAP II phosphorylation and that in some cell lines this change promotes viral late transcription.

L17 ANSWER 2 OF 32 MEDLINE
2000311224 Document Number: 20311224. PubMed ID: 10854163. Identification of the US3 gene product of BHV-1 as a protein kinase and characterization of BHV-1 **mutants** of the US3 gene. Takashima Y; Tamura H; Xuan X; Otsuka H. (Department of Global Agricultural Sciences, Graduate School of Agricultural and Life Science, The University of Tokyo, Japan.) VIRUS RESEARCH, (1999 Jan) 59 (1) 23-34. Journal code: X98; 8410979. ISSN: 0168-1702. Pub. country: Netherlands. Language: English.

AB We have identified the product of the US3 gene of bovine herpes virus type 1 (BHV-1), which is homologous to the herpes simplex virus type 1 (**HSV-1**) US3 protein kinase (PK) gene. The antibodies against the BHV-1 US3 gene product reacted with a 58 kDa **polypeptide** in BHV-1 infected cells and the 58 kDa **polypeptide** purified by immuno-precipitation demonstrated PK activity. Recent reports indicating that the US3 gene of **HSV-1** is involved in the blockage of apoptosis in virus infected cells. As to the apoptosis in BHV-1 infected cells, we found following: (1) no apoptosis was observed in cells infected with wild type BHV-1 and the US3 **mutants** (2) the apoptosis induced by the osmotic shock

of sorbitol treatment was blocked when cells were infected by the wild type BHV-1 (3) the US3 **mutants** of BHV-1 blocked the apoptosis of sorbitol treated cell, but the suppressive effect was delayed relative to that of wild type BHV-1 (4) the other BHV-1 **mutants**, with the intact US3 gene but with some other non-essential gene (genes) deleted behaved similar way to the US3 **mutant**. It is concluded that the US3 gene of BHV-1 is not directly involved in the blockage of apoptosis in infected cells.

L17 ANSWER 3 OF 32 MEDLINE

1998139088 Document Number: 98139088. PubMed ID: 9499048. Pseudorabies virus glycoprotein gK is a virion structural component involved in virus release but is not required for entry. Klupp B G; Baumeister J; Dietz P; Granzow H; Mettenleiter T C. (Institute of Molecular and Cellular Virology, Friedrich-Loeffler-Institutes, Federal Research Centre for Virus Diseases of Animals, Insel Riems, Germany.) JOURNAL OF VIROLOGY, (1998 Mar) 72 (3) 1949-58. Journal code: KCV; 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The pseudorabies virus (PrV) gene homologous to herpes simplex virus type 1 (**HSV-1**) UL53, which encodes **HSV-1** glycoprotein K (gK), has recently been sequenced (J. Baumeister, B. G. Klupp, and T. C. Mettenleiter, J. Virol. 69:5560-5567, 1995). To identify the corresponding protein, a rabbit antiserum was raised against a 40-kDa glutathione S-transferase-gK fusion protein expressed in Escherichia coli. In Western blot analysis, this serum detected a 32-kDa **polypeptide** in PrV-infected cell lysates as well as a 36-kDa protein in purified virion preparations, demonstrating that PrV gK is a structural component of virions. After treatment of purified virions with endoglycosidase H, a 34-kDa protein was detected, while after incubation with N-glycosidase F, a 32-kDa protein was specifically recognized. This finding indicates that virion gK is modified by N-linked glycans of complex as well as high-mannose type. For functional analysis, the UL53 open reading frame was interrupted after codon 164 by insertion of a gG-lacZ expression cassette into the wild-type PrV genome (PrV-gKbeta) or by insertion of the bovine herpesvirus 1 gB gene into a PrV gB- genome (PrV-gK(gB)). Infectious **mutant** virus progeny was obtained only on complementing gK-expressing cells, suggesting that gK has an important function in the replication cycle. After infection of Vero cells with either gK **mutant**, only single infected cells or small foci of infected cells were visible. In addition, virus yield was reduced approximately 30-fold, and penetration kinetics showed a delay in entry which could be compensated for by phenotypic gK complementation. Interestingly, the plating efficiency of PrV-gKbeta was similar to that of wild-type PrV on complementing and noncomplementing cells, pointing to an essential function of gK in virus egress but not entry. Ultrastructurally, virus assembly and morphogenesis of PrV gK **mutants** in noncomplementing cells were similar to wild-type virus. However, late in infection, numerous nucleocapsids were found directly underneath the plasma membrane in stages typical for the entry process, a phenomenon not observed after wild-type virus infection and also not visible after infection of gK-complementing cells. Thus, we postulate that presence of gK is important to inhibit immediate reinfection.

L17 ANSWER 4 OF 32 MEDLINE

96146729 Document Number: 96146729. PubMed ID: 8560762. The product of a 1.9-kb mRNA which overlaps the **HSV-1** alkaline nuclease gene (UL12) cannot relieve the growth defects of a null **mutant**. Martinez R; Shao L; Bronstein J C; Weber P C; Weller S K. (Department of Microbiology, University of Connecticut Health Center, Farmington 06030, USA.) VIROLOGY, (1996 Jan 15) 215 (2) 152-64. Journal code: XEA; 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB Alkaline nuclease, a relatively abundant viral phosphoprotein in herpes simplex virus type 1 (**HSV-1**)- or HSV-2-infected cells, is encoded by a 2.3-kb mRNA (R. H. Costa, K. G. Draper, L. Banks, K. L.

Powell, G. Cohen, R. Eisenberg, and E. K. Wagner, 1983. J. Virol. 48, 591-603). This mRNA is a member of a family of five unspliced 3'-coterminal messages. Costa et al. proposed that another member of this family of mRNAs (1.9-kb) may encode an N-terminally truncated protein which shares its carboxy-terminus with the alkaline nuclease protein. We previously described the isolation of AN-1, a deletion/insertion **mutant** of the alkaline nuclease gene (S. K. Weller, R. M. Seghatoleslami, L. Shao, D. Rowse, and E. P. Carmichael, 1990. J. Gen. Virol. 71, 2941-2952). The deletion in AN-1 would be predicted to abolish gene products of both the 2.3- and the 1.9-kb mRNAs. To investigate whether the putative truncated version of alkaline nuclease encoded by the 1.9-kb mRNA has enzymatic activity and plays a role in the viral life cycle, a viral **mutant** (AN-F1) was constructed which is predicted to abolish the gene product of the 2.3-kb mRNA (full-length alkaline nuclease) but leave intact the putative product of the 1.9-kb mRNA. Using a highly sensitive polyclonal antiserum raised against a bacterially expressed full-length alkaline nuclease, we observed a 60-kDa protein in KOS- and AN-F1-infected cells but not in AN-1-infected cells. This suggests that the 60-kDa protein is likely to be expressed from the 1.9-kb mRNA; the open reading frame is now designated UL12.5. Despite the presence of the 60-kDa band, AN-F1 failed to exhibit any alkaline exonuclease activity. This result suggests that the truncated **polypeptide** (UL12.5) is not enzymatically active, has low levels of activity, or possesses enzymatic activity which is not detected because of the low abundance of the **polypeptide**. AN-1 and AN-F1 are both severely restricted with respect to growth in Vero cells, as viral yields are 100- to 1000-fold lower than those of wild-type virus. We previously reported that the major defect in AN-1 is in the ability of DNA-containing capsids which form in the nucleus to mature into the cytoplasm (L. Shao, L. M. Rapp, and S. K. Weller, 1993. Virology 196, 146-162); AN-F1 exhibits the same defect. These results indicate that although the 1.9-kb mRNA encodes a 60-kDa protein presumably from the UL12.5 open reading frame, this **polypeptide** cannot substitute for the full-length UL12 product.

L17 ANSWER 5 OF 32 MEDLINE DUPLICATE 1

95266277 Document Number: 95266277. PubMed ID: 7747442. Transcriptional analysis of the short segment of the feline herpesvirus type 1 genome and insertional mutagenesis of a unique reading frame. Willemse M J; Strijdveen I G; van Schooneveld S H; van den Berg M C; Sondermeijer P J. (Virological Research Department, Intervet International B. V., Boxmeer, The Netherlands.) VIROLOGY, (1995 Apr 20) 208 (2) 704-11. Journal code: XEA; 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB Transcription mapping was performed in the short region of the feline herpesvirus type 1 (FHV-1) genome as a first approach to the functional analysis of open reading frames encoding the homologs of the herpes simplex virus type 1 (**HSV-1**) **gD**, gI, gE, US9, and probably also US8.5. All reading frames appeared to be transcribed. Transcripts were grouped into two nested RNA sets; namely, the coterminal transcripts of **gD** and gI and the coterminal transcripts of gE, US8.5, and US9. This situation was similar to that found in the equivalent region of **HSV-1**. The FHV-1 ORFs US8.5 and US9 have not been described previously. Sequence analysis and comparison of the putative **polypeptide** encoded by US8.5 revealed that this ORF was unique to FHV-1. However, US8.5 of FHV-1 might be functionally related to its positional homologs in **HSV-1** and equine herpesvirus type 1. In all three viruses, US8.5 does not seem to be critical for virus propagation in cell culture. This was shown for FHV-1 by isolating a **mutant** containing an insertion in US8.5 and comparing its growth properties in cell culture to those of the parent virus G2620. With regard to US9, conscientious amino acid sequence alignment of FHV-1 US9 and homologs in related herpesviruses suggests that this particular protein could contribute to the virus infectivity in vivo.

This speculation was based on the highly conserved C-terminus of US9, starting with a characteristic YYSES motif and followed by a nuclear target sequence and a transmembrane region.

L17 ANSWER 6 OF 32 MEDLINE DUPLICATE 2
95320971 Document Number: 95320971. PubMed ID: 7597804. Transcriptional analyses of the unique short segment of EHV-1 strain Kentucky A. Colle C F 3rd; O'Callaghan D J. (Department of Microbiology and Immunology, Louisiana State University Medical Center, Shreveport, USA.) VIRUS GENES, (1995 Feb) 9 (3) 257-68. Journal code: XEI; 8803967. ISSN: 0920-8569. Pub. country: United States. Language: English.

AB The unique short (Us) segment of the genome of equine herpesvirus type 1 (EHV-1) strain KyA is comprised of six open reading frames (ORFs) that encode: a) a homolog of the Us2 protein of herpes simplex virus type 1 (**HSV-1**); b) a serine threonine protein kinase that is a homolog of the **HSV-1** Us3 protein; c) a homolog of pseudorabies virus glycoprotein gX and HSV-2 gG; d) a novel glycoprotein, EUS4, not encoded by other herpesviruses sequenced to date; e) a homolog of **HSV-1 gD**; and f) a homolog of **HSV** **-1** Us9. The KyA strain is a deletion **mutant** that lacks Us sequences encoding gI, gE, and a potential 10 kD **polypeptide**, and thus may be useful as a parent virus for the generation of live virus vaccines. To complete the elucidation of the transcriptional program of the Us segment, Northern blot hybridization and S1 nuclease analyses were performed on poly(A)(+)-selected RNA isolated from infected cells maintained under early (phosphonoacetic acid-block) and late conditions. The findings revealed that the gene (EUS2 ORF) encoding the protein kinase is expressed as an early 2.9 kb transcript that overlaps and is 3' coterminal with a 1.6 kb early transcript that encodes the gG/gX homolog (EUS3 ORF). Two transcripts of 1.6 kb and 5.8 kb are 5' coterminal and may both encode the novel glycoprotein gene EUS4. The 1.6 kb transcript terminates at a poly(A) signal site downstream of the EUS4 ORF, and the 5.8 kb transcript terminates within the inverted repeat (IR) segment. Overall, the transcriptional program of the EHV-1 KyA Us segment is complex and exhibits similarities to that of **HSV-1** Us segment: a) transcripts arise from both DNA strands; b) some transcripts, including those mapping at the termini of the Us segment, extend into the IR segments and are 3' coterminal with the 1.2 kb IR6 transcript; c) at least one transcript reads through a functional polyadenylation signal; d) some transcripts encoding genes that lie in different reading frames exist as a family of overlapping mRNAs, some in an anti-sense manner. Lastly, of the six Us genes of the EHV-1 KyA strain, only those encoding the EHV-1 protein kinase and the HSV-2 gG/gX homolog are members of the early kinetic class.

L17 ANSWER 7 OF 32 MEDLINE
94201749 Document Number: 94201749. PubMed ID: 8151292. Characterization of the herpes simplex virus type 1 strain 17+ neurovirulence gene RL1 and its expression in a bacterial system. McKie E A; Hope R G; Brown S M; MacLean A R. (MRC Virology Unit, Institute of Virology, Glasgow, U.K.) JOURNAL OF GENERAL VIROLOGY, (1994 Apr) 75 (Pt 4) 733-41. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The DNA sequence of herpes simplex virus type 1 (**HSV-1**) strain 17+ in the region coding for the **polypeptide** ICP34.5 predicts a protein of 248 amino acids with a proposed M(r) of 26,158. The entire RL1 open reading frame was cloned into the expression vector pET8c to enable over-expression of ICP34.5 in Escherichia coli. The expressed protein was partially purified and used as an immunogen to produce a polyclonal antiserum in rabbits. Construction of an ICP34.5 null **mutant** (1771), demonstrated that the predicted open reading frame for ICP34.5 in strain 17+ is correct and confirmed that **HSV-** **1** strain 17+ ICP34.5 specifically determines neurovirulence. The specificity of the anti-serum directed against the E. coli-expressed

ICP34.5 was defined by Western blotting of wild-type and RL1-negative infected cell extracts.

L17 ANSWER 8 OF 32 MEDLINE

94378507 Document Number: 94378507. PubMed ID: 8091662. A genetic selection method for the transfer of **HSV-1** glycoprotein B mutations from plasmid to the viral genome: preliminary characterization of transdominance and entry kinetics of **mutant** viruses. Desai P; Homa F L; Person S; Glorioso J C. (Department of Molecular Genetics and Biochemistry, University of Pittsburgh, Pennsylvania 15261.) VIROLOGY, (1994 Oct) 204 (1) 312-22. Journal code: XEA; 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB A genetic selection procedure has been devised to transfer mutations from a plasmid to the viral genome. Reagents were constructed so that the recombination events that occur during cotransfection rescue a mutation in a recipient viral genome and, simultaneously, transfer a mutation in an adjacent (target) gene to the viral genome. In the example presented here the two adjacent genes are essential for viral replication, so that a transformed cell line that expresses both genes and another cell line that expresses only the target gene are required. Ideally the recipient viral genome should be deleted for the entire target gene, and the deletion should extend a short distance into the adjacent gene. In the present study UL27 (glycoprotein gB) of herpes simplex virus type 1 (KOS) is the target gene for mutation transfer and the upstream gene UL28, which specifies the ICP18.5 **polypeptide**, is the marker-rescue gene. A recipient virus that was deleted for DNA sequences encoding the C-terminal 74 residues of ICP18.5 and the N-terminal 711 residues of gB was constructed. All of the gB **mutant** plasmids used overlap the ICP18.5 deletion, and therefore, recombination events that rescue the ICP18.5 deletion must transfer a gB mutation present in codons 1-711 of the rescuing plasmid. Recombinant viruses that contain the gB mutation, unlike the parental gB-/18.5- virus, will grow on cells that express only gB (D6). This procedure has been used to transfer insertion, deletion, and chain termination mutations into the gB gene of the KOS genome. Southern blot analysis confirmed the transfer of the mutations to the viral genome. Analysis of radioactively labeled, infected cell lysates by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), before and after immune precipitation with gB-specific antibodies, confirmed the presence of the **mutant polypeptides** in the lysates. The incorporation of the **mutant polypeptides** into the envelopes of purified released viruses was measured. The yield of plaque forming units per cell was determined from single step growth curves after infection of permissive D6 cells. Virus yield, a measure of transdominance, varied for the different **mutants**. The maximum reduction in virus yield observed was sixfold relative to the wild-type virus. Transdominance was a result of both the lack of glycoprotein processing and the presence of gB-oligomerization sites. A reduced yield was also observed for a previously isolated gB-null **mutant** virus, K082. The amount of gB produced in D6 cells, infected with K082, was less than that produced in KOS infected cells, which may account for the reduced yield.(ABSTRACT TRUNCATED AT 400 WORDS)

L17 ANSWER 9 OF 32 MEDLINE

93383365 Document Number: 93383365. PubMed ID: 8396795. Inhibition of herpes simplex virus type 1 DNA replication by **mutant** forms of the origin-binding protein. Stow N D; Hammarsten O; Arbuckle M I; Elias P. (Medical Research Council Virology Unit, Institute of Virology, Glasgow, United Kingdom.) VIROLOGY, (1993 Oct) 196 (2) 413-8. Journal code: XEA; 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB The herpes simplex virus type 1 (**HSV-1**) origin-binding protein (OBP) is a sequence-specific DNA binding protein encoded by gene UL9 which interacts with the viral origins of DNA replication and also exhibits DNA helicase activity. Sequence-specific DNA binding activity has

previously been shown to reside within the C-terminal 317 amino acids, and when expressed alone, this domain exerts a dominant inhibitory effect on **HSV-1** DNA synthesis. We have tested several UL9 gene **mutants** for ability to support or interfere with viral DNA replication. **Mutants** affected in an ATP binding motif presumed to be associated with DNA helicase activity (ATP-), or defective in origin binding (OBP-) were unable to support replication in a transient assay for **HSV-1** origin-dependent DNA synthesis. When the products were screened for their ability to interfere with replication, the ATP- but not the OBP- **mutant** was inhibitory. Introduction of a mutation which abolished origin-binding activity into the isolated C-terminal fragment also removed the ability to interfere. The C-terminal fragment retained inhibitory activity when the wild-type (wt) protein was specified by a plasmid in which an OBP recognition site within the UL9 gene coding region had been mutated so as to prevent binding without affecting the encoded amino acids. These results suggest that in this assay inhibition of DNA synthesis probably results primarily from competition between **mutant** and wt forms of OBP for binding to the viral replication origins. The infectivity of **HSV-1** DNA in co-transfection experiments was greatly reduced by **mutant** UL9 proteins which interfered with origin-dependent DNA replication and also by high level expression of the wt **polypeptide**.

L17 ANSWER 10 OF 32 MEDLINE

93057368 Document Number: 93057368. PubMed ID: 1331297. Antiviral properties of a dominant negative **mutant** of the herpes simplex virus type 1 regulatory protein ICP0. Weber P C; Kenny J J; Wigdahl B. (Pennsylvania State University College of Medicine, Milton S. Hershey Medical Center, Department of Microbiology and Immunology, Hershey 17033.) JOURNAL OF GENERAL VIROLOGY, (1992 Nov) 73 (Pt 11) 2955-61. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Dominant negative or trans-dominant **mutants** of viral proteins represent a new and exciting potential approach to antiviral therapy. Unfortunately, the extreme specificity of a given dominant negative **mutant** limits its general utility in treating a broad spectrum of viral diseases, since it can typically interfere with the activity of only a single viral **polypeptide** encoded by a single virus. However, it seems likely that dominant negative **mutants** of promiscuous viral trans-activator proteins, which by definition would repress rather than activate gene expression, should be able to inhibit infectious virus production for a number of different viruses. One such dominant negative **mutant**, derived from the herpes simplex virus type 1 (**HSV -1**) regulatory protein ICP0, was found previously to behave as a powerful repressor of gene expression from an assortment of **HSV-1** and non-**HSV-1** promoters in transient expression assays. In the present study, this ICP0 **mutant** was found to be capable of inhibiting the replication of both **HSV-1** and a completely unrelated virus, human immunodeficiency virus, in cell culture. The properties of this dominant negative **mutant** indicate that it may have potential as a means of treating diseases caused by a number of DNA and RNA viruses. Moreover, a truncated form of ICP0 which can hypothetically be created by alternative splicing was found to possess similar inhibitory capabilities, suggesting that a virus-encoded version of this dominant negative **mutant** may play a role in down-regulating **HSV-1** gene expression during infection in vivo.

L17 ANSWER 11 OF 32 MEDLINE

92185462 Document Number: 92185462. PubMed ID: 1312117. The myristylated virion proteins of herpes simplex virus type 1: investigation of their role in the virus life cycle. MacLean C A; Dolan A; Jamieson F E; McGeoch D J. (MRC Virology Unit, University of Glasgow, U.K.) JOURNAL OF GENERAL VIROLOGY, (1992 Mar) 73 (Pt 3) 539-47. Journal code: I9B; 0077340. ISSN:

0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Herpes simplex virus type 1 (**HSV-1**) gene UL11 encodes a myristylated virion protein. In this paper we have characterized the UL11 product further and investigated its role in the virus life cycle. Wild-type **HSV-1** strain 17syn+ expresses three electrophoretically distinguishable UL11 **polypeptide** species. Analysis of single plaque isolates demonstrated that two virus populations exist within the 17syn+ stock: a major population encoding only the two higher Mr species, and a minor population encoding the lowest Mr species alone. DNA sequence analysis suggests that the latter **polypeptide** differs from the former ones at a single amino acid residue only. The UL11 **polypeptides** are synthesized as delayed early gene products and are phosphorylated in vitro. Following subcellular fractionation of infected cells, they are found predominantly associated with membranes. Within the virus particle, they appear to reside within the tegument. An insertion **mutant** containing the lacZ gene from Escherichia coli within the UL11 open reading frame is viable in tissue culture, although it gives smaller plaques and is impaired for growth compared to the wild-type parent or revertant viruses; it does not have a temperature-sensitive or host-range phenotype. Thus, although required for efficient replication, the myristylated **HSV-1** virion protein, in contrast to those of many other viruses, is not essential for virus growth in tissue culture.

L17 ANSWER 12 OF 32 MEDLINE

91170949 Document Number: 91170949. PubMed ID: 1848600. Construction and characterization of herpes simplex type 1 viruses without introns in immediate early gene 1. Everett R D. (MRC Virology Unit, Glasgow, U.K.) JOURNAL OF GENERAL VIROLOGY, (1991 Mar) 72 (Pt 3) 651-9. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Herpes simplex virus type 1 (**HSV-1**) encodes at least 70 distinct genes in a DNA genome sequence of about 150 kb. In contrast to most cellular genes and those of several other DNA viruses, the overwhelming majority of **HSV-1** transcripts are not spliced. One exception is immediate early (IE) gene 1, which contains two introns in the Vmw110 coding region. This study investigated the possibility that IE-1 intron sequences have a role during **HSV-1** infection. IE-1 genes lacking the first, second or both introns were constructed by site-directed deletion mutagenesis and recombined into the viral genome. Viruses lacking the IE-1 introns were essentially indistinguishable from the parent virus in terms of growth, particle to p.f.u. ratio or viral **polypeptide** expression in a variety of cell types. The lack of introns did not affect the time-course or efficiency of expression of Vmw110 either during normal infection or in cycloheximide reversal experiments. In contrast, in transfection assays, the loss of both intron sequences resulted in the elimination of the ability of a plasmid-encoded IE-1 to activate gene expression. These results imply that in certain situations the introns in IE-gene 1 may contribute to the efficient expression of Vmw110 but such an effect is not readily apparent using a recombinant virus in the tissue culture systems tested. In the course of this work a **mutant** of Vmw110 was fortuitously isolated which had lost the majority of an extremely acidic section of the **polypeptide**; this mutation appeared to have little effect on Vmw110 function.

L17 ANSWER 13 OF 32 MEDLINE

92024101 Document Number: 92024101. PubMed ID: 1656593. The **HSV-1** UL45 gene product is not required for growth in Vero cells. Visalli R J; Brandt C R. (Department of Medical Microbiology/Immunology, University of Wisconsin, Madison 53706.) VIROLOGY, (1991 Nov) 185 (1) 419-23. Journal code: XEA; 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB We have constructed a **HSV-1** UL45 null **mutant**

(UL45 delta) by inserting a TK-lacZ cassette into a BclI site near the 5' end of the UL45 gene. A polyclonal antiserum produced to an Escherichia coli trpE:UL45 fusion protein was used to show that an 18-kDa **polypeptide** corresponding to the predicted UL45 gene product was produced in **HSV-1** strain KOS-infected Vero cells but was not detected in UL45 delta-infected Vero cells. The absence of the 18-kDa protein had only a slight effect on viral growth in cell culture, indicating that the UL45 gene product is not essential for growth in Vero cells. However, the burst size of UL45 delta was smaller than **HSV-1** KOS in Vero and HeLa cells. UL45 delta also had a smaller plaque size and an altered plaque morphology.

L17 ANSWER 14 OF 32 SCISEARCH COPYRIGHT 2002 ISI (R)
91:66949 The Genuine Article (R) Number: EU573. PROTECTION AGAINST ZOSTERIFORM SPREAD OF HERPES-SIMPLEX VIRUS BY MONOCLONAL-ANTIBODIES. MESTER J C; GLORIOSO J C; ROUSE B T (Reprint). UNIV TENNESSEE, COLL VET MED, DEPT MICROBIOL, KNOXVILLE, TN, 37996; UNIV PITTSBURGH, SCH MED, DEPT MOLEC GENET & BIOCHEM, PITTSBURGH, PA, 15261. JOURNAL OF INFECTIOUS DISEASES (1991) Vol. 163, No. 2, pp. 263-269. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The in vivo protective role of herpes simplex virus (**HSV-1**)-specific antibody was analyzed using monoclonal antibodies (MAbs) reactive with discrete antigenic sites on glycoproteins B, C, and D (gB, gC, **gD**) in the murine zosteriform spread model of **HSV-1**. All of the anti-gC and anti-**gD** MAbs, and one of four anti-gB MAbs (B6) were protective. The in vitro abilities of the MAbs to neutralize **HSV-1** and mediate antibody-dependent cellular cytotoxicity (ADCC) against **HSV-1**-infected cells were examined as potential mechanistic correlates to in vivo protection. All animals given MAbs at high ADCC unit doses were protected. Some but not all mice given MAbs at high ADCC unit doses were protected. These studies designate specific epitopes recognized by protective antibodies and indicate that protection from the neurologic spread of HSV may be related to neutralization, ADCC, or both. The actual contribution of ADCC and neutralization to in vivo antibody-mediated protection remains unclear.

L17 ANSWER 15 OF 32 MEDLINE
91253261 Document Number: 91253261. PubMed ID: 1645902. Phenotypic and genotypic characterization of locus Syn 5 in herpes simplex virus 1. Tognon M; Guandalini R; Romanelli M G; Manservigi R; Trevisani B. (Institute of Biological Sciences, School of Medicine, University of Verona, Italy.) VIRUS RESEARCH, (1991 Mar) 18 (2-3) 135-50. Journal code: X98; 8410979. ISSN: 0168-1702. Pub. country: Netherlands. Language: English.
AB Previous papers have reported that the syncytial **mutant HSV-1**(13)S11 carries three segregable syn mutations and exhibits its altered phenotype in four different cell lines, i.e. HEp-2, VERO, BHK and HEL both at 34 degrees C and 39 degrees C. Those studies have shown that one of three syncytial loci, designated Syn 5, is located in the Bam HI Q fragment spanning map units 0.296-0.317 of the prototype arrangement. Recombinants obtained from marker transfer experiments with donor BamHI Q fragment, have shown that locus Syn 5 is able to induce cell-to-cell fusion in VERO, BHK and HEL but not in HEp-2 cells. In this paper we have characterized the syn **mutant HSV-1**(13)S11 with regard to plaque morphology, synthesis of viral **polypeptides** and glycoproteins, thymidine kinase activity and physical map position of locus Syn 5 on the genome. Pertinent to the syn phenotype, earlier papers claimed that two different **polypeptides**, thymidine kinase (TK) and glycoprotein H (gH), whose genes map in BamHI Q, may be responsible for the fusion activity. Functional studies on the TK of the syn **mutant HSV-1**(13)S11 indicate that this **polypeptide** accumulates normally in infected cells and

is a fully active enzyme. The other gene product, gH, has been studied with SDS-PAGE and in radioimmunoprecipitation (RIP) experiments using specific monoclonal antibodies. The results indicate that the amount of gH accumulation in the syn **mutant**-infected cells is greater than its parental strain. However, new marker transfer experiments described here located locus Syn 5 in 663 base pairs between SstI and EcoRI restriction endonuclease sites at the right end of the BamHI Q fragment, where TK gene overlaps in opposite orientation with UL 24 gene. Altogether these results indicate that the Syn 5 locus segregates from the gene specifying gH, to a region encompassing portions of the TK and UL 24 genes, and that the syn mutation does not affect the expression or activity of TK.

L17 ANSWER 16 OF 32 MEDLINE

90362064 Document Number: 90362064. PubMed ID: 2167931. A prominent serine-rich region in Vmw175, the major transcriptional regulator protein of herpes simplex virus type 1, is not essential for virus growth in tissue culture. Paterson T; Everett R D. (MRC Virology Unit, Glasgow, U.K.) JOURNAL OF GENERAL VIROLOGY, (1990 Aug) 71 (Pt 8) 1775-83. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Herpes simplex virus type 1 (**HSV-1**) encodes five immediate early (IE) genes of which at least three are involved in the transcriptional regulation of later classes of viral genes. Perhaps the most important of these regulatory proteins is Vmw175, a nuclear phosphoprotein of 1298 predicted amino acid residues. In the absence of functional Vmw175 the virus fails to activate early or late genes or to repress IE gene expression. All viruses of the sub-family alphaherpes-virinae encode **polypeptides** that are closely related to Vmw175. Mutational studies have shown that regions of homology within this family of gene regulators are generally of functional importance. One of the most striking conserved stretches of amino acid sequence is a run of serine residues followed by a highly acidic region in the amino-terminal fifth of the **polypeptide**. We have constructed an **HSV-1** virus which lacks this serine-rich run within Vmw175. Surprisingly, the virus was viable in tissue culture cells and expressed apparently normal amounts of viral **polypeptides**. In plaque assays it was very slightly temperature-sensitive and, depending on the state of the host cells, could generate plaques with a syncytial morphology. The **mutant** protein was able to bind to DNA in a manner indistinguishable from that of the wild-type **polypeptide**. We conclude that despite its conservation in all of the alphaherpes-virinae so far sequenced, the serine-rich homology is not important for virus growth in tissue culture.

L17 ANSWER 17 OF 32 MEDLINE

89381704 Document Number: 89381704. PubMed ID: 2550578. A herpes simplex virus type 1 **mutant** containing a deletion within immediate early gene 1 is latency-competent in mice. Clements G B; Stow N D. (Department of Virology, University of Glasgow, U.K.) JOURNAL OF GENERAL VIROLOGY, (1989 Sep) 70 (Pt 9) 2501-6. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB We have investigated the behaviour in mice of the herpes simplex virus type 1 (**HSV-1**) **mutant** dl1403, which contains a deletion within the gene encoding the immediate early **polypeptide** Vmw110. The deletion was responsible for a reduction in virulence assayed by both the intracranial and footpad routes of inoculation. Following injection into the footpad, dl1403 was able to reach the spinal cord and establish a latent infection in sensory ganglia from which virus spontaneously reactivated upon explanation. The Vmw110 **polypeptide** is therefore dispensable for the establishment and maintenance of latency and for reactivation from the latent state.

L17 ANSWER 18 OF 32 MEDLINE

89199774 Document Number: 89199774. PubMed ID: 2539510. Physical mapping and nucleotide sequence of a herpes simplex virus type 1 gene required for capsid assembly. Pertuiset B; Boccara M; Cebrian J; Berthelot N; Chousterman S; Puvion-Dutilleul F; Sisman J; Sheldrick P. (Institut de Recherches Scientifiques sur le Cancer, Villejuif, France.) JOURNAL OF VIROLOGY, (1989 May) 63 (5) 2169-79. Journal code: KCV; 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB In this report, we describe some phenotypic properties of a temperature-sensitive **mutant** of herpes simplex type 1 (**HSV-1**) and present data concerning the physical location and nucleotide sequence of the genomic region harboring the mutation. The effect of shifts from the permissive to the nonpermissive temperature on infectious virus production by the **mutant** A44ts2 indicated that the mutated function is necessary throughout, or late in, the growth cycle. At the nonpermissive temperature, no major differences were detected in viral DNA or protein synthesis with respect to the parent A44ts+. On the other hand, electron microscopy of **mutant** -infected cells revealed that neither viral capsids nor capsid-related structures were assembled at the nonpermissive temperature. Additional analyses employing the Hirt extraction procedure showed that A44ts2 is also unable to mature replicated viral DNA into unit-length molecules under nonpermissive conditions. The results of marker rescue experiments with intact A44ts2 DNA and cloned restriction fragments of A44ts+ placed the lesion in the coordinate interval 0.553 to 0.565 (1,837 base pairs in region UL) of the **HSV-1** physical map. No function has previously been assigned to this region, although it is known to be transcribed into two 5' coterminal mRNAs which code in vitro for a 54,000-molecular-weight **polypeptide** (K. P. Anderson, R. J. Frink, G. B. Devi, B. H. Gaylord, R. H. Costa, and E. K. Wagner, J. Virol. 37:1011-1027, 1981). We sequenced the interval 0.551 to 0.565 and found an open reading frame (ORF) for a 50,175-molecular-weight **polypeptide** . The predicted product of this ORF exhibits strong homology with the product of varicella-zoster virus ORF20 and lower, but significant, homology with the product of Epstein-Barr virus BORF1. For the three viruses, the corresponding ORFs lie just upstream of the gene coding for the large subunit of viral ribonucleotide reductase. The ORF described here corresponds to the ORF designated UL38 in the recently published nucleotide sequence of the **HSV-1** UL region (D. J. McGeoch, M. A. Dalrymple, A. J. Davison, A. Dolan, M. C. Frame, D. McNab, L. J. Perry, J. E. Scott, and P. Taylor, J. Gen. Virol. 69:1531-1574, 1988).

L17 ANSWER 19 OF 32 MEDLINE

89279294 Document Number: 89279294. PubMed ID: 2543774. Construction and characterization of herpes simplex virus type 1 **mutants** with defined lesions in immediate early gene 1. Everett R D. (MRC Virology Unit, Institute of Virology, Glasgow, U.K.) JOURNAL OF GENERAL VIROLOGY, (1989 May) 70 (Pt 5) 1185-202. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Transcription from the early and late classes of the herpes simplex virus type 1 (**HSV-1**) promoters requires prior immediate early (IE) gene expression. Although the product of IE gene 1, Vmw110, is not absolutely essential for virus growth in tissue culture, transfection experiments have demonstrated that Vmw110 can activate gene expression both by itself and in a synergistic manner with the product of IE gene 3, Vmw175. This paper describes the construction of 10 **mutant** **HSV-1** viruses with deletion and insertion mutations in Vmw110. The **mutant** viruses were then studied in single-step growth curve experiments, by assaying for plaques in a variety of cell types and by analysis of viral **polypeptide** synthesis during productive infection at high and low multiplicities. The results show that mutations in Vmw110 reduce the efficiency of plaque formation by **HSV-1**; the extent of this reduction depends on cell type and the position of the mutation in the **polypeptide**. In

particular, a potential zinc finger domain is crucial for Vmw110 function. The patterns and amounts of viral **polypeptide** synthesis during high multiplicity infections with **mutant** and wild-type viruses were similar in all cell types. At low multiplicity, mutations in Vmw110 reduced viral gene expression in the least permissive cell type. The data suggest that the role of Vmw110 during virus infection in tissue culture is at a very early stage of low multiplicity infections; its inactivity leads to the failure to express viral genes so that the virus does not enter the lytic cycle.

L17 ANSWER 20 OF 32 MEDLINE
89279248 Document Number: 89279248. PubMed ID: 2543754. Complementation of a herpes simplex virus type 1 Vmw110 deletion **mutant** by human cytomegalovirus. Stow E C; Stow N D. (MRC Virology Unit, Institute of Virology, Glasgow, U.K.) JOURNAL OF GENERAL VIROLOGY, (1989 Mar) 70 (Pt 3) 695-704. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The herpes simplex virus type 1 (**HSV-1**) **mutant** dl1403 contains a 2 kb deletion within the sequences encoding the immediate early **polypeptide** Vmw110. Previous experiments showed that although dl1403 exhibits normal patterns of gene expression following infection at an m.o.i. of 5 p.f.u./cell its growth and plaquing efficiency are impaired in low multiplicity infections, particularly in human foetal lung (HFL) cells. We have now investigated the ability of two other human herpesviruses, varicella-zoster virus (VZV) and human cytomegalovirus (HCMV), to compensate for this defect at low m.o.i. in HFL cells. Co-infection with HCMV resulted in greatly increased plaque numbers and the apparent particle/p.f.u. ratios of dl1403 stocks were reduced to values similar to those exhibited by wild-type **HSV-1** stocks. Complementation of dl1403 in low multiplicity infections by HCMV and VZV was also demonstrated by an increased yield of the **mutant** virus and an increase in synthesis of dl1403 DNA. Ultraviolet irradiation of HCMV abolished its ability to complement dl1403 and the presence of adenovirus 5 had no stimulatory effect on dl1403 DNA replication. When HFL monolayers were infected with dilutions of dl1403 stocks such that no plaques were produced, replication of the **mutant** virus could be induced by superinfection with HCMV 7 days after the initial infection. These results indicate that a non-lytic interaction between dl1403 and HFL cells is a more likely consequence of a low multiplicity infection than plaque formation.

L17 ANSWER 21 OF 32 MEDLINE DUPLICATE 3
89037346 Document Number: 89037346. PubMed ID: 2846873. Herpes simplex viruses lacking glycoprotein D are unable to inhibit virus penetration: quantitative evidence for virus-specific cell surface receptors. Johnson D C; Ligas M W. (Department of Pathology, McMaster University, Hamilton, Ontario, Canada.) JOURNAL OF VIROLOGY, (1988 Dec) 62 (12) 4605-12. Journal code: KCV; 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Herpes simplex virus (HSV) glycoprotein D (**gD**) plays an essential role in the entry of virus into cells. HSV **mutants** unable to express **gD** were constructed. The **mutants** can be propagated on VD60 cells, which supply the viruses with **gD**; however, virus particles lacking **gD** were produced in **mutant**-infected Vero cells. Virus particles with or without **gD** adsorbed to a large number (greater than 4 x 10(4] of sites on the cell surface; however, virions lacking **gD** did not enter cells. Cells pretreated with UV-inactivated virions containing **gD** (approximately 5 x 10(3) particles per cell) were resistant to infection with HSV type 1 (**HSV-1**) and HSV-2. In contrast, cells pretreated with UV-inactivated virions lacking **gD** could be infected with **HSV-1** and HSV-2. If infectious **HSV-1** was added prior to UV-inactivated virus particles containing **gD**, the infectious virus entered cells and

replicated. Therefore, virus particles containing **gD** appear to block specific cell surface receptors which are very limited in number. Particles lacking **gD** are presumably unable to interact with these receptors, suggesting that **gD** is an essential receptor-binding **polypeptide**.

L17 ANSWER 22 OF 32 MEDLINE
89010696 Document Number: 89010696. PubMed ID: 2844968. Mutational analysis of the herpes simplex virus type 1 trans-inducing factor Vmw65. Ace C I; Dalrymple M A; Ramsay F H; Preston V G; Preston C M. (Medical Research Council Virology Unit, Glasgow, U.K.) JOURNAL OF GENERAL VIROLOGY, (1988 Oct) 69 (Pt 10) 2595-605. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The herpes simplex virus type 1 (**HSV-1**) **polypeptide** Vmw65 is a structural component of the virus particle and is also responsible for trans-induction of immediate early (IE) transcription. Functional domains of this **polypeptide** were investigated by constructing a series of 10 plasmids each with a 12 bp insertion in the gene encoding Vmw65. Plasmids were analysed for their ability to stimulate IE transcription in short term transfection assays, and the altered Vmw65 **polypeptides** were assayed for the ability to form an IE-specific protein-DNA complex (IEC) in vitro. A direct correlation was observed between stimulation of transcription and formation of IEC, strongly suggesting that IEC is an important intermediate in transcription activation. Plasmids were also tested for their ability to rescue the temperature-sensitive mutation in the HSV-2 assembly **mutant** ts2203, since marker rescue analysis indicated that this mutation maps within the gene encoding Vmw65. Five plasmids failed to rescue ts2203, thereby defining regions of Vmw65 required for virus assembly. The results show that distinct domains exist in Vmw65 for activation of transcription and assembly of virus.

L17 ANSWER 23 OF 32 MEDLINE DUPLICATE 4
88004419 Document Number: 88004419. PubMed ID: 2820720. A detailed mutational analysis of Vmw110, a trans-acting transcriptional activator encoded by herpes simplex virus type 1. Everett R D. (MRC Virology Unit, Glasgow, UK.) EMBO JOURNAL, (1987 Jul) 6 (7) 2069-76. Journal code: EMB; 8208664. ISSN: 0261-4189. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Viral genes expressed during infection of tissue culture cells by herpes simplex virus type 1 (**HSV-1**) can be divided into three broad temporal groups called immediate-early (IE), early and late. Prior expression of IE gene products is required before later classes of genes can be transcribed. Using cloned copies of viral genes in plasmid vectors, it has been shown that the products of IE genes 1 and 3 (Vmw110 and Vmw175) can activate transcription from both viral and cellular promoters in short-term transfection assays. The effects of these two IE gene products are markedly synergistic in HeLa cells; the activation observed with both genes present is about 20 times that observed with Vmw175 alone. The mechanism of this activation and the properties of the IE proteins that are required are not well understood. This paper describes the construction of a large number of in-frame insertion and deletion mutations in a plasmid-encoded copy of IE gene 1. The ability of the **mutant** Vmw110 **polypeptides** to activate gene expression (in the presence of Vmw175) from the **HSV-1** glycoprotein **gD** promoter linked to the chloramphenicol acetyl transferase gene was studied. The results show that the structural integrity of at least five regions of the **polypeptide** are important for its function in the presence of Vmw175.

L17 ANSWER 24 OF 32 MEDLINE
87206162 Document Number: 87206162. PubMed ID: 3033824. Rapid identification of nonessential genes of herpes simplex virus type 1 by Tn5 mutagenesis. Weber P C; Levine M; Glorioso J C. SCIENCE, (1987 May 1) 236

(4801) 576-9. Journal code: UJ7; 0404511. ISSN: 0036-8075. Pub. country: United States. Language: English.

AB The large genome of herpes simplex virus type of (**HSV-1**) encodes at least 80 **polypeptides**, the majority of which have no recognized function. A subgroup of these gene products appears to be nonessential for virus replication in cell culture, but contributes to the complex life cycle of the virus in the host. To identify such functions, a simple insertional mutagenesis method has been used for selective inactivation of individual **HSV-1** genes. The bacterial transposon Tn5 was allowed to insert randomly into cloned restriction fragments representing the entire short unique (US) region of the **HSV-1** genome. Of the 12 open reading frames that were mutagenized with Tn5, **mutant** derivatives of US2, US4, and US5 were recombined into the virus. These three genes proved to be nonessential for **HSV-1** replication in Vero (African Green monkey kidney) cells and the US4 gene appeared to be involved in viral pathogenesis in the central nervous system of mice. This rapid mutagenesis procedure should prove useful in exploring the entire **HSV-1** genome as well as the genomes of other complex animal viruses.

L17 ANSWER 25 OF 32 MEDLINE

88044494 Document Number: 88044494. PubMed ID: 2823462. Genetic and phenotypic characterization of **mutants** in four essential genes that map to the left half of **HSV-1** UL DNA. Weller S K; Carmichael E P; Aschman D P; Goldstein D J; Schaffer P A. (Department of Microbiology, University of Connecticut Health Center, Farmington 06032.) VIROLOGY, (1987 Nov) 161 (1) 198-210. Journal code: XEA; 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB Several **HSV-1** proteins including the major capsid protein (VP5), two minor capsid proteins (VP11-12 and VP18.8), the alkaline nuclease and glycoprotein gH have been reported to be encoded by the left-most one-third of **HSV-1** UL DNA. In this paper, we present physical mapping data and phenotypic analysis of six ts **mutants** whose mutations lie within this region and which collectively represent four functional complementation groups (1-6, 1-7, 1-10, and 1-26). In this study, **mutants** in complementation group 1-10 were found to be defective in the synthesis of viral DNA, late viral **polypeptides**, and the formation of mature capsid-like structures--properties characteristic of other ts **mutants** defective in functions required for viral DNA synthesis. Two DNA-positive **mutants** in complementation group 1-7 fail to induce capsid formation and probably possess mutations in coding sequences for VP5. **Mutants** in two other complementation groups (1-6 and 1-26) synthesize significant levels of viral DNA, late **polypeptides**, and capsids. The functions of the gene products represented by these **mutants** remain to be determined.

L17 ANSWER 26 OF 32 MEDLINE

87085476 Document Number: 87085476. PubMed ID: 3025339. Isolation and characterization of a herpes simplex virus type 1 **mutant** containing a deletion within the gene encoding the immediate early **polypeptide** Vmw110. Stow N D; Stow E C. JOURNAL OF GENERAL VIROLOGY, (1986 Dec) 67 (Pt 12) 2571-85. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Transfection experiments with plasmids containing immediate early (IE) genes of herpes simplex virus type 1 (**HSV-1**) have previously demonstrated a role for the IE **polypeptide** Vmw110 (ICP0) in stimulating expression from plasmid-encoded early gene promoters. To gain further insights into the function of Vmw110 we isolated a deletion **mutant** specifying a truncated form of the **polypeptide** which had been shown to be inactive in transfection assays. This **mutant**, dl1403, contained a 2 kb deletion within both the TRL and IRL copies of the Vmw110 gene, and encoded a

polypeptide consisting of the original N-terminal 105 amino acids followed by 56 amino acids specified by a reading frame not used by Vmw110. dl1403 was able to replicate and produce plaques on baby hamster kidney (BHK) cells but the yield of infectious virus was 20- to 100-fold lower than obtained with wild-type **HSV-1**. Surprisingly, comparison of **polypeptide** synthesis, DNA replication and DNA encapsidation in cells infected with 5 p.f.u./cell dl1403 or wild-type **HSV-1** revealed no significant differences. In addition similar numbers of particles were produced in cells infected with the two viruses, resulting in stocks of dl1403 exhibiting significantly higher particle/p.f.u. ratios. The efficiency of plaquing of dl1403 was greatly reduced in Vero and human foetal lung cells compared with BHK cells, but following infection with 5 p.f.u./cell similar yields of infectious virus were obtained from all three cell lines. Marker rescue experiments verified that the reduced yield of dl1403 in BHK cells was a consequence of the deletion within the Vmw110 gene. The results suggest that the effect of this deletion is manifest primarily at low multiplicities of infection and can be largely overcome by increasing the virus dose.

L17 ANSWER 27 OF 32 MEDLINE

86114025 Document Number: 86114025. PubMed ID: 3003243. An in vitro latency system for herpes simplex virus type 2. Russell J; Preston C M. JOURNAL OF GENERAL VIROLOGY, (1986 Feb) 67 (Pt 2) 397-403. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB An in vitro latency system for herpes simplex virus type 2 (HSV-2) in cultured cells has been developed. Virus replication was suppressed by infection of human foetal lung cells at the supraoptimal temperature of 42 degrees C, and, following transfer of such cell cultures to the normal growth temperature of 37 degrees C, infectious virus was generally undetectable for at least 6 days. HSV-2 was reactivated by intertypic superinfection at 38.5 degrees C with temperature-sensitive **mutants** of **HSV-1**, or with human cytomegalovirus, but not by superinfection with adenovirus types 2 or 5. The **HSV-1 mutant** tsKsyn, which produces only immediate early **polypeptides** at 38.5 degrees C, was as effective as the late **mutant** tsIsyn, but tsK which had been irradiated with u.v. light to prevent gene expression did not reactivate HSV-2. The efficiency of reactivation was very high, since 15 to 34% of the theoretical input of infectious HSV-2 particles could be retrieved by superinfection with 0.3 p.f.u. of tsKsyn per cell. Reactivation of latent virus was not induced by cell subculture or by other treatments which alter cell metabolism. The system described here may be important for studies on the molecular basis of HSV latency.

L17 ANSWER 28 OF 32 MEDLINE

84137575 Document Number: 84137575. PubMed ID: 6321636. Isolation and characterization of revertants from fourteen herpes simplex virus type 1 (strain 17) temperature-sensitive **mutants**. Dargan D J; Subak-Sharpe J H. JOURNAL OF GENERAL VIROLOGY, (1984 Mar) 65 (Pt 3) 477-91. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The isolation of spontaneous non-temperature-sensitive revertants of herpes simplex virus type 1 (**HSV-1**) (strain 17) ts **mutants**, following a single round of selection at non-permissive temperature, is reported. The distinction between total and incomplete reversion was assessed by the wild-type performance of non-ts revertants in three aspects of HSV infection: (i) virus growth, (ii) induction of HSV-specified enzyme activities (where appropriate) and (iii) the gel profile of infected cell **polypeptides**. Wild-type behaviour was taken to indicate total reversion, while less than wild-type performance in any test indicated incomplete reversion. Only five of 19 **HSV-1 mutants** (ts L, U, X, R and G syn) examined for

reversion of the ts lesion failed to yield non-ts revertants; these **mutants** may well contain multiple mutations. Total reversion was obtained with **mutants** ts K, F, E, S, M, N and I and incomplete reversion with the **mutants** ts D, T, B, P, A, W, F, H and possibly K. Thus, both total and incomplete revertants of ts F (and possibly ts K) were obtained. Some conclusions concerning the relative importance of individual **polypeptide** bands have been drawn from these studies. Within our sample in the revertant profiles Vmw 175, 155, 114, 65/64, 43, 40, 39, 30, 28, 21 and 16.5K always returned to wild-type levels; Vmw 273, 100, 67 and 38/37K almost always regained wild-type intensity but **polypeptides** Vmw 122, 117, 82/81, 57, 51, 27 and 12.5K were frequently not made in wild-type amounts.

L17 ANSWER 29 OF 32 MEDLINE DUPLICATE 5

83199210 Document Number: 83199210. PubMed ID: 6189286. Inhibition of glycosylation of herpes simplex virus glycoproteins: identification of antigenic and immunogenic partially glycosylated glycopeptides on the cell surface membrane. Glorioso J; Szczesiul M S; Marlin S D; Levine M. VIROLOGY, (1983 Apr 15) 126 (1) 1-18. Journal code: XEA; 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB The surface membranes of cells infected with herpes simplex virus type 1 (**HSV-1**), strain KOS, contain three principal glycoproteins, gC (apparent Mr 129k), gB (apparent Mr 120k), and **gD** (apparent Mr 58k). Infections carried out in the presence of the glycosylation inhibitor 2-deoxy-D-glucose result in the loss of the mature species with the concurrent appearance of lower-molecular-weight **polypeptides** which are presumably partially glycosylated forms of the fully processed glycoproteins. Specific immunoprecipitation of radiolabeled cytoplasmic extracts of 2-deoxy-D-glucose-inhibited infections identified partially glycosylated proteins designated DG92, DG88, and DG53, which are antigenically related to the corresponding mature forms gB, gC, and **gD**. Cell surface radioiodination, in combination with specific immunoprecipitation, revealed that DG88 and DG53 were the principal species transported to the cell surface in 2-deoxy-D-glucose-inhibited infections. DG92 was readily detected in the cytoplasm but not on the plasma membrane. Cells infected with the KOS **mutant**, syn LD70, did not synthesize glycoprotein gC. In glycosylation-inhibited syn LD70 infections, DG88 was not detected in either the cytoplasm or plasma membrane, demonstrating a genetic relationship between DG88 and gC. Polyclonal and monoclonal antibodies directed against the glycoproteins gC, gB, and **gD** sensitized infected cells to complement-mediated immune cytolysis. Cells infected in the presence of the inhibitor were sensitized to lysis only by antibody specific for gC and **gD**. The glycosylation-inhibited cells were insensitive to immunolysis by anti-gB monoclonal antibody. These findings confirm that the glycosylation-deficient forms of gC and **gD**, but not gB reach the cell surface in the presence of inhibitor and that the inhibitor-induced alterations in glycosylation do not cause a complete loss of antigenicity. Inoculation of mice with syngeneic 3T3 cells infected in the presence or absence of inhibitor-induced cytolytic and neutralizing antibody. A major portion of the cytolytic antibody was directed against gC, but anti-gC antibody appeared to play a minor role in virus neutralization. While the serum induced by the control infected cells contained precipitating antibodies for gC, gB, and **gD**, the serum derived from mice inoculated with inhibitor-treated infected cells had only weak immunoprecipitating activity against gB. Together, these findings have identified partially glycosylated forms of the major HSV glycoproteins and show that complete glycosylation is not required for transport of some of these partially glycosylated **polypeptides** to the cell surface. Moreover, complete glycosylation of the glycopeptides is not essential for maintenance of antigenicity or immunogenicity, indicating that at least some determinants recognized by antibodies directed against the mature glycoproteins are not affected by 2-deoxy-D-glucose-induced carbohydrate alterations.

L17 ANSWER 30 OF 32 MEDLINE

83110913 Document Number: 83110913. PubMed ID: 6296278. Thymidine kinase deletion **mutants** of herpes simplex virus type 1. Sanders P G; Wilkie N M; Davison A J. JOURNAL OF GENERAL VIROLOGY, (1982 Dec) 63 (2) 277-95. Journal code: I9B; 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Deletions in the cloned thymidine kinase (TK) gene of herpes simplex virus type 1 (**HSV-1**), strain 17 syn+, were produced by two methods. Removal of a 506 base pair fragment from between the unique SstI and Bg/II restriction endonuclease sites of pTK1 (**HSV-1** BamHI p cloned in pAT153) and subsequent transformation of Escherichia coli resulted in the isolation of 50 deleted plasmids. Sequential digestion of pTK1 with Bg/II and nuclease BAL 31 followed by ligation and recleavage with Bg/II resulted in the isolation of 31 deleted plasmids. Three clones, pTK2, pTK3 and pTK4, obtained following Bg/II and SstI treatment of pTK1 were recombined with wild-type (wt) **HSV-1** (17) syn+ DNA in baby hamster kidney (BHK) cells to produce TK- deletion **mutants HSV-1** (17) TK 1301, **HSV-1** (17) TK 1302 and **HSV-1** (17) TK 1303 respectively. 5-Bromo-2'-deoxyuridine, 5-bromo-2'-deoxycytidine and 9-(2-hydroxyethoxymethyl)guanine were used to reduce the background of TK+ virus in heterogeneous recombinant stocks analysed for the presence of TK- recombinants. All recombinant clones isolated produced a small syncytial plaque morphology in BHK cells. The **mutants HSV-1** (17) TK 1301 and **HSV-1** (17) TK 1302 were TK-, failed to produce **polypeptides** of molecular weights 43000 and 19000 found in wt-infected cells and demonstrated one-step growth curves different from wt virus and the TK- **mutant HSV-1** (17) dPyk-7. Superinfection studies with **HSV-1** (17) TK 1301, **HSV-1** (17) TK 1302, **HSV-1** (MDK) and **HSV-1** (17) dPyk-7 indicated that all TK- **mutants** except dPyK-7 produce a trans-acting gene product which can switch on the transforming **HSV-1** TK gene.

L17 ANSWER 31 OF 32 MEDLINE

77097287 Document Number: 77097287. PubMed ID: 189089. Herpes simplex virus resistance and sensitivity to phosphonoacetic acid. Honess R W; Watson D H. JOURNAL OF VIROLOGY, (1977 Feb) 21 (2) 584-600. Journal code: KCV; 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Phosphonoacetic acid (PAA) inhibited the synthesis of herpes simplex virus DNA in infected cells and the activity of the virus-specific DNA polymerase in vitro. In the presence of concentrations of PAA sufficient to prevent virus growth and virus DNA synthesis, normal amounts of early virus proteins (alpha- and beta-groups) were made, but late virus proteins (gamma-group) were reduced to less than 15% of amounts made in untreated infected cells. This residual PAA-insensitive synthesis of gamma-**polypeptides** occurred early in the virus growth cycle when rates were identical in PAA-treated and untreated infected cells. Passage of virus in the presence of PAA resulted in selection of **mutants** resistant to the drug. Stable clones of **mutant** viruses with a range of drug sensitivities were isolated and the emergence of variants resistant to high concentrations of PAA involved the sequential selection of **mutants** progressively better adapted to growth in the presence of the drug. Increased drug resistance of virus yield or plaque formation was correlated with increased resistance of virus DNA synthesis, gamma-protein synthesis, and resistance of the virus DNA polymerase reaction in vitro to the inhibitory effects of the drug. PAA-resistant strains of herpes simplex virus type 1 (**HSV-1**) complemented the growth of sensitive strains of homologous and heterologous types in mixed infections in the presence of the drug. Complementation was markedly dependent upon the proportions of the

resistant and sensitive partners participating in the mixed infection. Intratypic (HSV-1A X HSV-1B) recombination of the PAA resistance marker(s), Pr, occurred at high frequency relative to plaque morphology (syn) and bromodeoxyuridine resistance (Br, thymidine kinase-negative phenotype) markers, with the most likely order being syn-Br-Pr. Recombinant viruses were as resistant or sensitive to PAA as the parental viruses, and viruses recombinant for their PAA resistance phenotype were also recombinant for the PAA resistance character of the virus DNA polymerase. The results provide additional evidence that the herpesvirus DNA polymerase is the site of action of PAA and illustrate the potential usefulness of PAA-resistant **mutants** in genetic studies of herpesviruses.

L17 ANSWER 32 OF 32 MEDLINE
76002154 Document Number: 76002154. PubMed ID: 169028. Viral gene functions expressed and detected by temperature-sensitive **mutants** of herpes simplex virus. Benyesh-Melnick M; Schaffer P A; Courtney R J; Esparza J; Kimura S. COLD SPRING HARBOR SYMPOSIA ON QUANTITATIVE BIOLOGY, (1975) 39 Pt 2 731-46. Journal code: DMT; 1256107. ISSN: 0091-7451. Pub. country: United States. Language: English.

AB The expression of HSV-specific gene functions by 22 ts **mutants** of **HSV-1** in 15 complementation groups and 8 ts **mutants** of HSV-2 in 7 complementation groups has been studied at the nonpermissive temperature. Four cistrons of **HSV-1** and three cistrons of HSV-2 with defects in viral DNA and DAN polymerase synthesis were identified. DNA-**mutants** of **HSV-1** revealed a greater alteration in HSV **polypeptide** synthesis and viral assembly than DNA- **mutants** of HSV-2. **Mutants** with apparent defects in structural proteins have been identified for both **HSV-1** and HSV-2 as demonstrated by their increased themolability. The general organization of the provisional **HSV-1** and HSV-2 linkage maps revealed a similarity in the arrangement of functionally related cistrons, with DNA- **mutants** being located on the left-hand side of each map and **mutants** with phenotypic properties similar to those of the wild-type virus, on the right-hand side. An early **polypeptide** of HSV (VP175, MW 175,000) was found to accumulate in cells infected at the nonpermissive temperature withts **mutants** of **HSV-1** in complementation group B. The VP175 **polypeptide** was isolated from such cells by a combination of SDS-preparative and analytical disc gel electrophoresis. Antiserum prepared to this **polypeptide** was found to descriminate between **HSV-1** and HSV-2 by immunofluorescence. On the other hand, type-specific gene functions of **HSV-1** and HSV-2 were not demonstrated through intertypic complementation and recombination tests with heterologous **mutant** pairs, whereas mutually exchangeable or common gene functions were readily identified. Eight ts **mutants** of HSV-2 were used to detect functional HSV genes in hamster embryo cells transformed by HSV-2. Normal hamster cells and SV40-transformed hamster cells failed to support the replication of the **mutants** at the nonpermissive temperature. However, the replication of two **mutants**, defective in late functions, was significantly enhanced in two independently derived HSV-2-transformed cell lines. Thus functional HSV genetic information was detected in HSV-2-transformed cells through the use of ts **mutants**. Moreover, it appears that the information present in both cell lines is not only specific but involves late HSV functions.

=> s autoimmune disease
L18 97970 AUTOIMMUNE DISEASE

=> s l18 and rheumatoid arthritis
L19 8989 L18 AND RHEUMATOID ARTHRITIS

=> s l1 and "p30" polypeptide
L20 0 L1 AND "P30" POLYPEPTIDE

=> s l19 and soluble ligand
L21 0 L19 AND SOLUBLE LIGAND

=> s l19 and method
L22 1633 L19 AND METHOD

=> s l22 and inhibit
L23 69 L22 AND INHIBIT

=> s l23 lymphocyte
MISSING OPERATOR L23 LYMPHOCYTE
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l23 and lymphocyte
L24 31 L23 AND LYMPHOCYTE

=> s l24 and proliferation
L25 18 L24 AND PROLIFERATION

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PROCESSING COMPLETED FOR L25
L26 11 DUP REMOVE L25 (7 DUPLICATES REMOVED)

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L26 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2002 ACS
2002:10532 Document No. 136:84702 Novel ligands for CD28 and CTLA-4 created by shuffling of mammalian B7-1 ligand cDNAs with possible therapeutic use as co-stimulatory molecules. Punnonen, Juha; Lazetic, Alexandra L. L.; Leong, Steven R.; Chang, Chia-Chun Jean; Apt, Doris; Gustafsson, Claes (Maxygen, Inc., USA). PCT Int. Appl. WO 2002000717 A2 20020103, 364 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US19973 20010622. PRIORITY: US 2000-PV213946 20000623; US 2000-PV241245 20001017.

AB The invention provides polynucleotides and polypeptides encoded therefrom having advantageous properties, including an ability of the polypeptides to preferentially bind a CD28 or CTLA-4 receptor at a level greater or less than the ability of human B7-1 to bind CD28 or CTLA-4, or to induce or **inhibit** altered level of T cell **proliferation** response greater compared to that generated by human B7-1. The polypeptides and polynucleotides of the invention are useful in therapeutic and prophylactic treatment **methods**, gene therapy applications, and vaccines. Novel ligands were generated by shuffling of sequences from cDNAs for B7-1 ligands from human, rhesus monkey, baboon, orangutan, cow, cat and rabbit. Ligands were screened for using a FACS assay. CDNA libraries were introduced into animal cells that were then screened for their ability to bind a labeled CD28 or CTLA-4 using FACS. Clones were screened for their preferential binding of CD28 vs. CTLA-4. Candidate clones were then tested for their ability to stimulate T cell **proliferation**.

L26 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2002 ACS

2001:798538 Document No. 135:340697 Cloning and characterization of G protein-coupled receptor G2A gene and its use in the diagnosis and treatment and drug screening of T cell hyperproliferation related diseases. Weng, Zhigang; Witte, Owen N. (Regents of the University of California, USA). PCT Int. Appl. WO 2001081918 A1 20011101, 104 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US12005 20010411. PRIORITY: US 2000-553875 20000420.

AB The invention relates to a G protein-coupled receptor (GPCR), called G2A, whose expression is regulated and functions at the G2/M checkpoint to ensure properly controlled duplication of hematopoietic cells. The receptor is found predominantly in hematopoietic cells and tissues and functions as a tumor suppressor gene and induces cell cycle arrest and integrates diverse signals by modulation of cytoskeletal architecture. G2A induced cytoskeletal rearrangement (assembly of actin stress fibers) is RhoA-dependent which is mediated by G.alpha.13. Human G2A gene is localized to chromosome 14q32.3. T cell derived from G2A knockout mice (G2A-/-) has increased **proliferation** and enhanced tyrosine protein phosphorylation. G2A plays an important role in regulating the **proliferation** and differentiation of lymphoid cells esp. T cells and regulation of G2A activity has therapeutic applications. **Methods** for identifying compds. which **inhibit** T cell hyperproliferation, and for diagnosis and treatment of related cancers and diseases are also disclosed.

L26 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2002 ACS

2001:781125 Document No. 135:343309 Ligand p30/LIGHT for HVEM (herpes virus entry mediator) and **methods** of therapeutic use. Ware, Carl F. (La Jolla Institute for Allergy and Immunology, USA). PCT Int. Appl. WO 2001079496 A2 20011025, 104 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US11857 20010411. PRIORITY: US 2000-524325 20000313; US 2000-549096 20000412.

AB A novel polypeptide ligand, p30, for HVEM (herpes virus entry mediator) and functional variations and fragments thereof are provided. The HVEM ligand is isolated from II-23.D7 cell line, a human CD4+ T cell hybridoma. P30, which can be found as a membrane protein and can function as a cytokine, is also called LIGHT, because this polypeptide is homologous to Lymphotoxins, exhibits Inducible expression, and competes with HSV Glycoprotein D for HVEM, a receptor expressed by T **lymphocytes**. Because LIGHT can compete with HSV glycoprotein D for HVEM, homo-trimeric sol. forms of this polypeptide can be used to block the entry of herpesvirus into cells. P30 is useful for modulating immune responses and in inhibiting infection and/or subsequent **proliferation** by herpesvirus. LIGHT also bind to the lymphotoxin-.beta. receptor (LT.beta.R). The present invention is also based upon the discovery that HVEM polypeptides have an antagonistic effect on inflammation. In particular, HVEM fusion proteins are capable of inhibiting inflammation when administered to a subject. HVEM-Fc fusion proteins are also provided. **Methods** for treating subjects with lymphoid cell disorders, tumors, **autoimmune diseases**, inflammatory disorders of those having or suspected of having a herpes virus infection,

utilizing p30 and the fusion proteins of the invention, are also provided.

L26 ANSWER 4 OF 11 MEDLINE DUPLICATE 1
2001058202 Document Number: 20491153. PubMed ID: 11035201. Linear and cyclic LFA-1 and ICAM-1 peptides **inhibit** T cell adhesion and function. Tibbetts S A; Seetharama Jois D; Siahaan T J; Benedict S H; Chan M A. (Department of Molecular Biosciences, University of Kansas, Lawrence, KS 66045, USA.) PEPTIDES, (2000 Aug) 21 (8) 1161-7. Journal code: PA7. ISSN: 0196-9781. Pub. country: United States. Language: English.
AB Short peptides derived from functional proteins have been used in several instances to **inhibit** activity of the parent proteins. In some cases, stability and efficacy were found to be increased by cyclization of these peptides. Inhibition of interaction of the two cell adhesion counter receptors leukocyte function-associated antigen (LFA)-1 and intercellular adhesion molecule (ICAM)-1 is being studied as a **method** for modulating **autoimmune diseases** such as **rheumatoid arthritis** and for facilitating organ transplantation. Here, several 10-amino acid peptides derived from the contact domains of LFA-1 and ICAM-1 were evaluated for their ability to interfere with intercellular adhesion by T cells and to **inhibit** a more biologic, mixed **lymphocyte** reaction. Both linear and cyclic forms of the peptides were effective at inhibiting intercellular adhesion. Cyclic forms were effective at inhibiting T cell activation and **proliferation** in the mixed **lymphocyte** reaction.

L26 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2002 ACS
1999:487210 Document No. 131:125455 Compositions and **methods** using a sphingomyelin signal transduction pathway inhibitor for treating **autoimmune diseases**. Holoshitz, Joseph; Shayman, James A.; Tan, Shi-Yu (The Regents of the University of Michigan, USA). PCT Int. Appl. WO 9937298 A1 19990729, 49 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US1117 19990120. PRIORITY: US 1998-9906 19980121.
AB **Methods** and compns. are described for treating and diagnosing **autoimmune diseases**, and in particular for treating and detecting **rheumatoid arthritis**. Treatment is described with a new class of anti-RA drug, namely compds. that **inhibit proliferation** and induce apoptosis. Compds. of the invention include inhibitors of the sphingomyelin signal transduction pathway.

L26 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2002 ACS
1999:249091 Document No. 130:262125 Use of a chemically stabilized chlorite solution for inhibiting an antigen-specific immune response. Kuhne, Frederich W.; McGrath, Michael; Engleman, Edgar G. (Oxo Chemie A.-G., Switz.). PCT Int. Appl. WO 9917787 A2 19990415, 44 pp. DESIGNATED STATES: W: AU, CA, CN, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-IB1676 19981006. PRIORITY: US 1997-60953 19971006.
AB **Methods** of using a stabilized chlorite soln. to **inhibit** antigen-specific immune responses are disclosed. The stabilized chlorite soln., when administered to a mammal in need thereof, can prevent the presentation of antigens by antigen-presenting cells. The stabilized chlorite soln. is therefore useful in treating e.g. **autoimmune diseases**, diseases caused by an inappropriate immune response, and lymphoproliferative disease, and in inhibiting rejection in transplant patients.

L26 ANSWER 7 OF 11 SCISEARCH COPYRIGHT 2002 ISI (R)
1999:770814 The Genuine Article (R) Number: 242KE. Peptides derived from ICAM-1 and LFA-1 modulate T cell adhesion and immune function in a mixed **lymphocyte** culture. Tibbetts S A; Chirathaworn C; Nakashima M; Jois D S S; Siahaan T J; Chan M A; Benedict S H (Reprint). UNIV KANSAS, DEPT MICROBIOL, LAWRENCE, KS 66045 (Reprint); UNIV KANSAS, DEPT MICROBIOL, LAWRENCE, KS 66045; UNIV KANSAS, DEPT PHARMACEUT CHEM, LAWRENCE, KS 66045. TRANSPLANTATION (15 SEP 1999) Vol. 68, No. 5, pp. 685-692. Publisher: LIPPINCOTT WILLIAMS & WILKINS. 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106. ISSN: 0041-1337. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background. The counter receptors intercellular adhesion molecule (ICAM)-1 and **lymphocyte** function-associated antigen (LFA)-1 are **lymphocyte** cell surface adhesion proteins the interaction of which can provide signals for T cell activation. This binding event is important in T cell function, migration, and general immune system regulation. The ability to **inhibit** this interaction with monoclonal antibodies has proved to be therapeutically useful for several allograft rejection and **autoimmune disease** models.

Methods. Short peptides representing counter-receptor contact domains of LFA-1 and ICAM-1 were examined for their ability to **inhibit** T cell adhesion and T cell function.

Results. Peptides encompassing amino acids Q1-C21 and D26-K50 of ICAM-1, I237-I261 and G441-G466 of the LFA-1 alpha-subunit, and D134-Q159 of the LFA-1 beta-subunit inhibited LFA-1/ICAM-1-dependent adhesion in a phorbol-12,13-dibutyrate-induced model of tonsil T cell homotypic adhesion. This inhibition was specific to the peptide sequence and occurred without stimulation of T cell **proliferation**. The peptides also were effective in preventing T cell function using a one-way mixed **lymphocyte** reaction model for bone marrow transplantation.

Conclusions. Our data suggest that these peptides or their derivatives may be useful as therapeutic modulators of LFA-1/ICAM-1 interaction during organ transplants.

L26 ANSWER 8 OF 11 MEDLINE DUPLICATE 2
1999114767 Document Number: 99114767. PubMed ID: 9918235. Mechanism of immunosuppression of the antirheumatic herb TWHf in human T cells. Ho L J; Chang D M; Chang M L; Kuo S Y; Lai J H. (Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, Republic of China.) JOURNAL OF RHEUMATOLOGY, (1999 Jan) 26 (1) 14-24. Journal code: JWX; 7501984. ISSN: 0315-162X. Pub. country: Canada. Language: English.

AB OBJECTIVE: To investigate the immunosuppressive mechanism of Tripterygium wilfordii Hook-F (TWHf) in human T cells. TWHf, a traditional Chinese medicinal herb for **rheumatoid arthritis**, has been shown to **inhibit** the function of immune effector cells such as neutrophils, macrophages, and B **lymphocytes**. **METHODS**: T cell survival was evaluated with trypan blue exclusion assay, morphologic changes with Wright's stain, the induction of endonuclease activity with DNA fragmentation assay, and the subdiploid DNA content with flow cytometry. T cell activation was measured with interleukin 2 (IL-2) ELISA and the expression of several surface molecules with flow cytometry. RESULTS: At high dosages, TWHf caused inhibition of T cell **proliferation** and this mechanism was mediated through the induction of apoptosis. TWHf, in noncytotoxic dosages, was as potent as cyclosporin A and more potent than prednisolone and cyclophosphamide in inhibiting IL-2 production from activated T cells. TWHf also inhibited both phorbol 12-myristate 13-acetate induced IL-2Ralpha expression and ionomycin induced CD40 ligand expression. TWHf did not reverse downregulated expression of CD3 and CD4 by phorbol ester stimulation. CONCLUSION: This is the first evidence that the immunosuppressive mechanism of TWHf in T cells was mediated through both downregulation of T cell receptor signaling pathway and induction of cellular apoptosis, which is defective in **autoimmune diseases**.

L26 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2002 ACS
1997:563324 Document No. 127:214810 A peptide therapy for **autoimmune diseases**: immunization with a peptide containing a dominant T cell determinant can protect mice from collagen-induced arthritis. Ametani, A.; Matsumoto, T.; Iwaya, A.; Kano, H.; Honda, A.; Hachimura, S.; Nakagami, T.; Kaminogawa, S. (Department of Applied Biological Chemistry, The University of Tokyo, Bunkyo, 113, Japan). Anim. Cell Technol.: Basic Appl. Aspects, Proc. Annu. Meet. Jpn. Assoc. Anim. Cell Technol., 8th, Meeting Date 1995, 493-499. Editor(s): Funatsu, Kazumori; Shirai, Yoshihito; Matsushita, Taku. Kluwer: Dordrecht, Neth. (English) 1997. CODEN: 64WUA2.

AB Collagen-induced arthritis (CIA) is a disease model of human **rheumatoid arthritis** useful for analyzing autoimmunity. This disease can be induced in DBA/1J mice injected with bovine type II collagen (bCII) plus adjuvant. In this study we synthesized bCII peptide 245-270 (p245-270), known to contain an immunodominant T cell determinant, and investigated the effect of peptide-preimmunization on the onset of CIA. When mice were preimmunized with this peptide plus complete Freund's adjuvant (CFA) H37Ra before injection with bCII plus incomplete adjuvant, the onset of CIA was much delayed, compared with other groups of mice (1) not preinjected, (2) preinjected with only CFA, or (3) preinjected with p316-333 plus CFA, before bCII-injection. The IgG1 and IgG2a antibody response to bCII was not suppressed in these mice preimmunized with p245-270. On the other hand, RT-PCR anal. of cytokine mRNA expression in lymph node cells (LNC) revealed that p245-270-preimmunization induced IL-4 expression in response to this peptide antigen, while bCII-injection did not. ELISA anal. of supernatants and **proliferation** assays of LNC indicated that secretion of one of the inflammatory cytokines relevant to CIA, IFN-.gamma., was not inhibited by p245-270-preimmunization, although **proliferation** was inhibited. Th2-type (IL-4-producing) p245-270-specific T cells did not **inhibit** the subsequent Th1-type response (IFN-.gamma. prodn.), suggesting that the inhibition of CIA did not result from the cross-regulation of cytokine prodn. patterns by Th1/Th2 cells. These observations imply that another mechanism for suppressing CIA is activated by preimmunization with this peptide. This activation protocol using an immunodominant peptide could be a new **method** of peptide immunotherapy for **autoimmune diseases**.

L26 ANSWER 10 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1996:288609 Document No.: PREV199699010965. Synthesis of alpha-glucosidase I inhibitors showing antiviral (HIV-1) and immunosuppressive activity. Van Den Broek, L. A. G. M. (1); Kat-Van Den Nieuwenhof, M. W. P.; Butters, T. D.; Van Boeckel, C. A. A.. (1) Scientific Development Group, Dep. Medicinal Chemistry, N. V. Organon, PO Box 20, 5340 BH Oss Netherlands. Journal of Pharmacy and Pharmacology, (1996) Vol. 48, No. 2, pp. 172-178. ISSN: 0022-3573. Language: English.

AB The synthesis of a series of analogues of the monosaccharide alpha-glucosidase I inhibitor N-decyl-1-deoxynojirimycin (1) is described. With the incorporation of a single oxygen atom particularly at position seven in the N-decyl side chain, i.e. to give N-7-oxadecyl-dNM (4), the therapeutic ratio (alpha-glucosidase I inhibitory activity over toxicity in HepG2 cells) increases considerably. N-7-Oxadecyl-dNM **inhibits** purified porcine liver alpha-glucosidase I with an IC50 value of 0.28 mu-M. The position of the oxygen atom in the N-decyl side chain is of importance since N-3-oxadecyl-dNM is less active and, moreover, is toxic to HepG2 cells at 3 m. Subsequently, the synthesis of a disaccharide inhibitor of sbd glucosidase I is described. The aminodisaccharide ManNH-2-alpha-1,2Glc (12) **inhibits** alpha-glucosidase I with an IC50 value of 15.7 mu-M. Two closely related monosaccharide derivatives of 12 did not **inhibit** the enzyme at low mu-m concentrations (no inhibition at 5 mu-M), showing the additional effect of binding of the aglycon fragment of the molecule to the active site of alpha-glucosidase

1. Next, the N-alkyl-dNM derivatives were analysed for antiviral and immunomodulatory activity in-vitro. It is found that the most potent alpha-glucosidase I inhibitor from this study, N-7-oxadecyl-dNM (4) **inhibits** HIV-1 induced syncytia formation and **lymphocyte proliferation** in-vitro. Finally, compound 4 was also investigated in-vivo. N-7-Oxadecyl-dNM (4) reduced adjuvant-induced arthritis in rats making this compound a potential candidate for treating **autoimmune diseases** like **rheumatoid arthritis**.

L26 ANSWER 11 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1996:81712 Document No.: PREV199698653847. Mechanism of the antiproliferative action of leflunomide: A77 1726, the active metabolite of leflunomide, does not block T-cell receptor-mediated signal transduction but its antiproliferative effects are antagonized by pyrimidine nucleosides. Cao, Wei W.; Kao, Peter N.; Chao, Anthony C.; Gardner, Phyllis; Ng, James; Morris, Randall E. (1). (1) Lab. Transplantation Immunol., CVRB 5247, Dep. Cardiothoracic Surg., Sch. Med., Stanford Univ., Stanford, CA 94305-5247 USA. Journal of Heart and Lung Transplantation, (1995) Vol. 14, No. 6 PART 1, pp. 1016-1030. ISSN: 1053-2498. Language: English.

AB Background: Leflunomide, a novel immunosuppressive drug, prolongs experimental graft survival effectively and has been well tolerated in patients with **rheumatoid arthritis**. A77 1726, the active metabolite of leflunomide, **inhibits lymphocyte proliferation** in vitro. This study was conducted in Jurkat T cells to investigate the effects of A77 1726 on signal transduction pathways initiated by ligands of the T-cell receptor CD3 complex and to evaluate the effects of A77 1726 on nucleotide biosynthesis. **Methods**: Tritiated thymidine incorporation and cell counts quantitated cell **proliferation**. Spectrofluorescence of Indo/AM dye measured intracellular Ca-2+ mobilization. A luciferase assay quantitated interleukin-2 gene promoter activity in stimulated cells transfected with an interleukin-2 promoter-luciferase gene construct. Pyrimidine and purine nucleosides were used to assess antagonism of the antiproliferative activity of A77 1726. Results: (1) A77 1726 dose-dependently inhibited the **proliferation** of Jurkat T cells (inhibitory concentration of 50% = 6 mu-mol/L); (2) A77 1726 did not decrease mobilization of intracellular Ca-2+ stimulated by phytohemagglutinin or anti-CD3 monoclonal antibody; (3) A77 1726 did not **inhibit** interleukin-2 gene promoter activity in cells stimulated with ionomycin plus phorbol myristate acetate; (4) inhibition of cell **proliferation** by A77 1726 was antagonized by addition of uridine, cytidine, or 2'-deoxycytidine; (5) addition of uridine 24 hours after treatment with A77 1726 antagonized inhibition of **proliferation**; (6) A77 1726 was not antagonized by 2'-deoxyuridine, thymidine, adenosine, or guanosine. Conclusions: (1) A77 1726 inhibited Jurkat T-cell **proliferation** without inhibiting T-cell receptor-mediated signal transduction events, including tyrosine kinase-dependent intracellular Ca-2+ mobilization and activation of the interleukin-2 gene promoter; (2) the antiproliferative effects of A77 1726 on Jurkat T cells are primarily due to interruption of de novo pyrimidine nucleotide biosynthesis. These data provide evidence for a novel in vitro mechanism of the antiproliferative action of this immunosuppressant.

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=> s ware c?/au
L27         973 WARE C?/AU

=> s l27 and "p30 polypeptide"
L28           0 L27 AND "P30 POLYPEPTIDE"

=> s l27 and HVEM
L29          17 L27 AND HVEM

=> dup remove l29
PROCESSING COMPLETED FOR L29
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L30 13 DUP REMOVE L29 (4 DUPLICATES REMOVED)

=> d l30 1-13 cbib abs

L30 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2002 ACS
2001:781125 Document No. 135:343309 Ligand p30/LIGHT for **HVEM** (herpes virus entry mediator) and methods of therapeutic use. **Ware, Carl F.** (La Jolla Institute for Allergy and Immunology, USA). PCT Int. Appl. WO 2001079496 A2 20011025, 104 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US11857 20010411. PRIORITY: US 2000-524325 20000313; US 2000-549096 20000412.

AB A novel polypeptide ligand, p30, for **HVEM** (herpes virus entry mediator) and functional variations and fragments thereof are provided. The **HVEM** ligand is isolated from II-23.D7 cell line, a human CD4+ T cell hybridoma. P30, which can be found as a membrane protein and can function as a cytokine, is also called LIGHT, because this polypeptide is homologous to Lymphotoxins, exhibits Inducible expression, and competes with HSV Glycoprotein D for **HVEM**, a receptor expressed by T lymphocytes. Because LIGHT can compete with HSV glycoprotein D for **HVEM**, homo-trimeric sol. forms of this polypeptide can be used to block the entry of herpesvirus into cells. P30 is useful for modulating immune responses and in inhibiting infection and/or subsequent proliferation by herpesvirus. LIGHT also bind to the lymphotoxin-.beta. receptor (LT.beta.R). The present invention is also based upon the discovery that **HVEM** polypeptides have an antagonistic effect on inflammation. In particular, **HVEM** fusion proteins are capable of inhibiting inflammation when administered to a subject. **HVEM** -Fc fusion proteins are also provided. Methods for treating subjects with lymphoid cell disorders, tumors, autoimmune diseases, inflammatory disorders of those having or suspected of having a herpes virus infection, utilizing p30 and the fusion proteins of the invention, are also provided.

L30 ANSWER 2 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)
2001:870593 The Genuine Article (R) Number: 480UY. The TNFR family member **HVEM** plays a role in thymic selection processes. Rickert S (Reprint); Granger S W; Kronenberg M; **Ware C E**. La Jolla Inst Allergy & Immunol, Div Mol Immunol, San Diego, CA 92121 USA; La Jolla Inst Allergy & Immunol, Div Dev Immunol, San Diego, CA 92121 USA. JOURNAL OF LEUKOCYTE BIOLOGY (30 OCT 2001) Supp. [S], pp. 101-101. MA 359. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA. ISSN: 0741-5400. Pub. country: USA. Language: English.

L30 ANSWER 3 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)
2001:870469 The Genuine Article (R) Number: 480UY. LIGHT interferes with the **HVEM**-mediated route of Herpes Simplex-1 infection.. Whitmire J (Reprint); Mauri D; Eisenberg R; Cohen G; Spear P; **Ware C**. La Jolla Inst Allergy & Immunol, San Diego, CA USA; Univ Penn, Philadelphia, PA 19104 USA; Northwestern Univ, Chicago, IL 60611 USA. JOURNAL OF LEUKOCYTE BIOLOGY (30 OCT 2001) Supp. [S], pp. 71-72. MA 234. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA. ISSN: 0741-5400. Pub. country: USA. Language: English.

L30 ANSWER 4 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2001:253282 Document No.: PREV200100253282. Ligand for herpes simplex virus entry mediator and methods of use. **Ware, Carl E. (1)**. (1) Solana Beach, CA USA. ASSIGNEE: La Jolla Institute for Allergy and Immunology, La Jolla, CA, USA. Patent Info.: US 6140467 October 31, 2000. Official

Gazette of the United States Patent and Trademark Office Patents, (Oct. 31, 2000) Vol. 1239, No. 5, pp. No Pagination. e-file. ISSN: 0098-1133. Language: English.

AB A novel ligand (p30) for herpes virus entry mediator, **HVEM**, is provided. p30 is useful for modulating immune responses and in inhibiting infection by herpes virus. Methods for treating subjects with lymphoid cell disorders or those having or suspected of having a herpes virus infection, utilizing p30 of the invention, are also provided.

L30 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2002 ACS

1999:64836 Document No. 130:138304 Ligand for herpes simplex virus entry mediator and methods of use. **Ware, Carl F.** (La Jolla Institute for Allergy and Immunology, USA). PCT Int. Appl. WO 9902563 A1 19990121, 61 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US13897 19980707. PRIORITY: US 1997-51964 19970707; US 1997-898234 19970730.

AB A novel ligand (p30) for herpes virus entry mediator (**HVEM**, exhibiting homol. to tumor necrosis factor receptor superfamily) is provided. The **HVEM** ligand is isolated from II-23.D7 cell line, a human CD4+ T cell hybridoma. P30 is useful for inhibiting infection by herpes virus and for modulating immune responses and therefore treating **HVEM**-assocd. disorders such as autoimmune disease, leukemia and lymphoma. GD and lymphotoxin .alpha. (LT.alpha.) are also **HVEM** binding agent like p30. Methods for treating subjects with lymphoid cell disorders or those having or suspected of having a herpes virus infection, utilizing p30 of the invention, are also provided.

L30 ANSWER 6 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)

1998:762711 The Genuine Article (R) Number: 121HC. LIGHT, a new pro-apoptotic cytokine member of the TNF superfamily, and lymphotoxin-alpha are ligands for the herpesvirus entry mediator (**HVEM**).. Mauri D (Reprint); Ebner R; Montgomery R; Kochel K; Cheung T C; Yu G L; Ruben S; Murphy M; Eisenberg R J; Cohen G H; Spear P G; **Ware C F**. LA JOLLA INST ALLERGY & IMMUNOL, SAN DIEGO, CA 92121; HUMAN GENOME SCI INC, ROCKVILLE, MD 20850; NORTHWESTERN UNIV, CHICAGO, IL 60611; UNIV PENN, PHILADELPHIA, PA 19104. FASEB JOURNAL (17 MAR 1998) Vol. 12, No. 4, Part 1, Supp. [S], pp. 1754-1754. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998. ISSN: 0892-6638. Pub. country: USA. Language: English.

L30 ANSWER 7 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

1998:200127 Document No.: PREV199800200127. Light, a new pro-apoptotic cytokine member of the TNF superfamily, and lymphotoxin-alpha are ligands for the herpesvirus entry mediator (**HVEM**. Mauri, D. (1); Ebner, R.; Montgomery, R.; Kochel, K. (1); Cheung, T. C. (1); Yu, G.-L.; Ruben, S.; Murphy, M.; Eisenberg, R. J.; Cohen, G. H.; Spear, P. G.; **Ware, C. F. (1)**. (1) La Jolla Inst. Allergy and Immunol., San Diego, CA 92121 USA. FASEB Journal, (March 17, 1998) Vol. 12, No. 4, pp. A301. Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 98, Part 1 San Francisco, California, USA April 18-22, 1998 Federation of American Societies for Experimental Biology. ISSN: 0892-6638. Language: English.

L30 ANSWER 8 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)

1998:891021 The Genuine Article (R) Number: 136CD. Light, a new lymphotoxin-related cytokine that engages the LT beta receptor and herpesvirus entry mediator (**HVEM**). **Ware C F (Reprint)** ; Butrovich K D; Mauri D N; Tillman J; Rooney I. LA JOLLA INST ALLERGY &

IMMUNOL, SAN DIEGO, CA 92121. EUROPEAN CYTOKINE NETWORK (SEP 1998) Vol. 9, No. 3, pp. 285-285. Publisher: JOHN LIBBEY EUROTEXT LTD. 127 AVE DE LA REPUBLIQUE, 92120 MONTROUGE, FRANCE. ISSN: 1148-5493. Pub. country: USA. Language: English.

L30 ANSWER 9 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1998:458033 Document No.: PREV199800458033. Production and purification of a recombinant, soluble form of light, a new member of the TNF superfamily. Rooney, I. A.; Mauri, D. N.; Cheung, T. C.; **Ware, C. F.**. La Jolla Inst. Allergy Immunol., San Diego, CA USA. Journal of Interferon and Cytokine Research, (May, 1998) Vol. 18, No. 5, pp. A44. Meeting Info.: 7th International Conference on Tumor Necrosis Factor and Related Molecules Scientific Advances and Medical Applications Hyannis, Massachusetts, USA May 17-21, 1998 ISSN: 1079-9907. Language: English.

L30 ANSWER 10 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1998:458030 Document No.: PREV199800458030. Light is a new member of the TNF superfamily that binds the herpesvirus entry mediator (**HVEM**) and the LTbeta receptor. Mauri, D. (1); Montgomery, R.; Rooney, I. (1); Kochel, K. (1); Cheung, T. C. (1); Ebner, Reinhard; Eisenberg, R. J.; Cohen, G. H.; Spear, P. G.; **Ware, C. F. (1)**. (1) La Jolla Inst. Allergy Immunol., San Diego, CA 92121 USA. Journal of Interferon and Cytokine Research, (May, 1998) Vol. 18, No. 5, pp. A43. Meeting Info.: 7th International Conference on Tumor Necrosis Factor and Related Molecules Scientific Advances and Medical Applications Hyannis, Massachusetts, USA May 17-21, 1998 ISSN: 1079-9907. Language: English.

L30 ANSWER 11 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1998:458017 Document No.: PREV199800458017. Lymphotoxins meet herpesvirus: New light on the darkside of virus-host interactions. **Ware, C. F. (1)** ; Mauri, D. M. (1); Ebner, R.; Montgomery, R. I.; Kochel, K. D. (1); Cheung, T. C. (1); Yu, G.-L.; Ruben, S.; Murphy, M.; Eisenberg, R. J.; Cohen, G. H.; Spear, P. G.. (1) La Jolla Inst. Allergy Immunol., San Diego, CA 92121 USA. Journal of Interferon and Cytokine Research, (May, 1998) Vol. 18, No. 5, pp. A36. Meeting Info.: 7th International Conference on Tumor Necrosis Factor and Related Molecules Scientific Advances and Medical Applications Hyannis, Massachusetts, USA May 17-21, 1998 ISSN: 1079-9907. Language: English.

L30 ANSWER 12 OF 13 MEDLINE DUPLICATE 1
1998122340 Document Number: 98122340. PubMed ID: 9462508. LIGHT, a new member of the TNF superfamily, and lymphotoxin alpha are ligands for herpesvirus entry mediator. Mauri D N; Ebner R; Montgomery R I; Kochel K D; Cheung T C; Yu G L; Ruben S; Murphy M; Eisenberg R J; Cohen G H; Spear P G; **Ware C F**. (Division of Molecular Immunology, La Jolla Institute for Allergy and Immunology, San Diego, California 92121, USA.) IMMUNITY, (1998 Jan) 8 (1) 21-30. Journal code: CCF; 9432918. ISSN: 1074-7613. Pub. country: United States. Language: English.

AB Herpes simplex virus (HSV) 1 and 2 infect activated T lymphocytes by attachment of the HSV envelope glycoprotein D (gD) to the cellular herpesvirus entry mediator (**HVEM**), an orphan member of the tumor necrosis factor receptor superfamily. Here, we demonstrate that **HVEM** binds two cellular ligands, secreted lymphotoxin alpha (LTalpha) and LIGHT, a new member of the TNF superfamily. LIGHT is a 29 kDa type II transmembrane protein produced by activated T cells that also engages the receptor for the LTalphabeta heterotrimer but does not form complexes with either LTalpha or LTbeta. HSV1 gD inhibits the interaction of **HVEM** with LIGHT, and LIGHT and gD interfere with **HVEM** -dependent cell entry by HSV1. This characterizes herpesvirus gD as a membrane-bound viokine and establishes LIGHT-**HVEM** as integral components of the lymphotoxin cytokine-receptor system.

L30 ANSWER 13 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1998:69400 Document No.: PREV199800069400. Lymphotoxin (LT)-alpha is a ligand

for the Herpes virus entry mediator (**HVEM**), a member of the TNF receptor family involved in activation of T and B cells. Mauri, D. (1); Kochel, K. (1); Cheung, T. C. (1); Montgomery, R.; Eisenberg, R. J.; Cohen, G. H.; Spear, P. G.; **Ware, C. F. (1)**. (1) La Jolla Inst. Allergy Immunology, San Diego, CA 92121 USA. Cytokine, (Nov., 1997) Vol. 9, No. 11, pp. 913. Meeting Info.: Fifth Annual Conference of the International Cytokine Society Lake Tahoe, Nevada, USA November 9-13, 1997 International Cytokine Society. ISSN: 1043-4666. Language: English.

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(FILE 'HOME' ENTERED AT 15:32:32 ON 25 FEB 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 15:32:47 ON 25 FEB 2002

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L1      9785672 S METHOD
L2            0 S L1 AND "P30 POLYPEPTIDE"
L3           45 S "P30" POLYPEPTIDE
L4            0 S L3 AND INHIBIT T CELL PROLIFERATION
L5           21 DUP REMOVE L3 (24 DUPLICATES REMOVED)
L6            2 S "HVEM" POLYPEPTIDE
L7            2 DUP REMOVE L6 (0 DUPLICATES REMOVED)
L8          516 S LYMPHOTOXIN BETA RECEPTOR
L9           71 S L8 AND SOLUBLE
L10           5 S L9 AND T CELL PROLIFERATION
L11           2 DUP REMOVE L10 (3 DUPLICATES REMOVED)
L12      283726 S "GD"
L13        3312 S L12 AND POLYPEPTIDE
L14         164 S L13 AND HSV-1
L15          47 S L14 AND MUTANT
L16           0 S L15 AND CELL PROLIFERATION
L17          32 DUP REMOVE L15 (15 DUPLICATES REMOVED)
L18       97970 S AUTOIMMUNE DISEASE
L19        8989 S L18 AND RHEUMATOID ARTHRITIS
L20           0 S L1 AND "P30" POLYPEPTIDE
L21           0 S L19 AND SOLUBLE LIGAND
L22        1633 S L19 AND METHOD
L23          69 S L22 AND INHIBIT
L24          31 S L23 AND LYMPHOCYTE
L25          18 S L24 AND PROLIFERATION
L26          11 DUP REMOVE L25 (7 DUPLICATES REMOVED)
L27         973 S WARE C?/AU
L28           0 S L27 AND "P30 POLYPEPTIDE"
L29          17 S L27 AND HVEM
L30          13 DUP REMOVE L29 (4 DUPLICATES REMOVED)

=>  s l27 and autoimmune disease
L31          12 L27 AND AUTOIMMUNE DISEASE

=> dup remove l31
PROCESSING COMPLETED FOR L31
L32           8 DUP REMOVE L31 (4 DUPLICATES REMOVED)

=> d l32 1-8 cbib abs

L32  ANSWER 1 OF 8     MEDLINE
2001700059  Document Number: 21615092.    PubMed ID: 11748255.   Turning on
     LIGHT. Granger S W; Ware C F. (Division of Molecular Immunology,
     La Jolla Institute for Allergy and Immunology, San Diego, California
     92121, USA. ) JOURNAL OF CLINICAL INVESTIGATION, (2001 Dec) 108 (12)
     1741-2.  Journal code: 7802877. ISSN: 0021-9738. Pub. country: United
     States. Language: English.
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L32 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS
2001:781125 Document No. 135:343309 Ligand p30/LIGHT for HVEM (herpes virus entry mediator) and methods of therapeutic use. **Ware, Carl F.** (La Jolla Institute for Allergy and Immunology, USA). PCT Int. Appl. WO 2001079496 A2 20011025, 104 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US11857 20010411. PRIORITY: US 2000-524325 20000313; US 2000-549096 20000412.

AB A novel polypeptide ligand, p30, for HVEM (herpes virus entry mediator) and functional variations and fragments thereof are provided. The HVEM ligand is isolated from II-23.D7 cell line, a human CD4+ T cell hybridoma. P30, which can be found as a membrane protein and can function as a cytokine, is also called LIGHT, because this polypeptide is homologous to Lymphotoxins, exhibits Inducible expression, and competes with HSV Glycoprotein D for HVEM, a receptor expressed by T lymphocytes. Because LIGHT can compete with HSV glycoprotein D for HVEM, homo-trimeric sol. forms of this polypeptide can be used to block the entry of herpesvirus into cells. P30 is useful for modulating immune responses and in inhibiting infection and/or subsequent proliferation by herpesvirus. LIGHT also bind to the lymphotoxin-.beta. receptor (LT.beta.R). The present invention is also based upon the discovery that HVEM polypeptides have an antagonistic effect on inflammation. In particular, HVEM fusion proteins are capable of inhibiting inflammation when administered to a subject. HVEM-Fc fusion proteins are also provided. Methods for treating subjects with lymphoid cell disorders, tumors, **autoimmune diseases**, inflammatory disorders of those having or suspected of having a herpes virus infection, utilizing p30 and the fusion proteins of the invention, are also provided.

L32 ANSWER 3 OF 8 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2002004799 EMBASE Turning on LIGHT. Granger S.W.; **Ware C.F.**. C.F. Ware, Division of Molecular Immunology, La Jolla Inst. for Allergy/Immun., 10355 Science Center Drive, San Diego, CA 92121, United States. carl_ware@liai.org. Journal of Clinical Investigation 108/12 (1741-1742) 2001.
Refs: 19.
ISSN: 0021-9738. CODEN: JCINAO. Pub. Country: United States. Language: English.

L32 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS
1999:64836 Document No. 130:138304 Ligand for herpes simplex virus entry mediator and methods of use. **Ware, Carl F.** (La Jolla Institute for Allergy and Immunology, USA). PCT Int. Appl. WO 9902563 A1 19990121, 61 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US13897 19980707. PRIORITY: US 1997-51964 19970707; US 1997-898234 19970730.

AB A novel ligand (p30) for herpes virus entry mediator (HVEM, exhibiting homol. to tumor necrosis factor receptor superfamily) is provided. The HVEM ligand is isolated from II-23.D7 cell line, a human CD4+ T cell hybridoma. P30 is useful for inhibiting infection by herpes virus and for modulating immune responses and therefore treating HVEM-assocd. disorders such as **autoimmune disease**, leukemia and lymphoma. GD

and lymphotoxin .alpha. (LT.alpha.) are also HVEM binding agent like p30. Methods for treating subjects with lymphoid cell disorders or those having or suspected of having a herpes virus infection, utilizing p30 of the invention, are also provided.

L32 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS
1996:572027 Document No. 125:204510 Controlling TRAF-mediated signals. Kieff, Elliott; Mosialos, George; Birkenbach, Mark; Vanarsdale, Todd; **Ware, Carl**; Kaye, Kenneth M. (Brigham & Women's Hospital, USA; Regents of the University of California). PCT Int. Appl. WO 9620723 A1 19960711, 86 pp. DESIGNATED STATES: W: JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US16980 19951228. PRIORITY: US 1994-367540 19941230.
AB Compds. and methods are presented for interrupting the interaction between Epstein-Barr virus-encoded proteins known as LMP1 and Tumor Necrosis Factor Receptor-Assocd. Factors (TRAFs), particularly novel human TRAFs, thereby inhibiting lymphoblast growth and tumorigenesis, particularly of Hodgkin's disease, Burkitt's lymphoma, lymphomas seen in immunocompromised patients (including AIDS-assocd. central nervous system lymphomas), and nasopharyngeal carcinomas. Therapies for treating EBV infection are also disclosed, e.g. in patients with infectious mononucleosis, by blocking the establishment of latent infection and/or blocking lytic infection. Compds. and methods for controlling TRAF-Mediated TNF/TNFR signaling by administering to a TRAF-encoding cell a compd. that inhibits TRAF oligomerization are also disclosed, as well as compds. and methods for controlling cell growth and death based on the interaction of TNF receptor family carboxy terminal cytoplasmic domains with human TRAFs, e.g., LAP1 and EBI6. These interactions are particularly important in controlling cells in the immune system and regulating immune responses. They are also important for controlling abnormally growing cells, that is cancer cells.

L32 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1995:521223 Document No.: PREV199598535523. Cytokine regulation of class II expression by activated T cells: Tumor necrosis factor alpha (TNF-alpha) upregulates HLA-DR expression, while lymphotoxin alpha (LT-alpha) and gamma interferon (INF-gamma) have no effect. Reiff, Andreas (1); **Ware, Carl F.**; Burotto, Felix; Arora, Yogesh K.; Walker, Sharyn M.. (1) Children's Hosp. Los Angeles, Univ. Southern Calif., Los Angeles, CA 90027 USA. Arthritis & Rheumatism, (1995) Vol. 38, No. 9 SUPPL., pp. S272. Meeting Info.: 59th National Scientific Meeting of the American College of Rheumatology and the 30th National Scientific Meeting of the Association of Rheumatology Health Professionals San Francisco, California, USA October 21-26, 1995 ISSN: 0004-3591. Language: English.

L32 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS
1994:603367 Document No. 121:203367 Lymphotoxin-.beta. and its therapeutic uses. Browning, Jeffrey; **Ware, Carl F.** (Biogen, Inc., USA; University of California). PCT Int. Appl. WO 9413808 A2 19940623, 111 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1993-US11669 19931202. PRIORITY: US 1992-990304 19921204.
AB Lymphotoxin-.beta. (LT-.beta.), a membrane protein of lymphocytes and a no. of other cell types including phorbol ester (PMA) stimulated T cell hybridoma II-23.D7 cells, is isolated and characterized and a cDNA encoding it is cloned and expressed. Lymphotoxin-.beta. forms complexes with other peptides such as lymphotoxin-.alpha. (LT-.alpha.) and also forms homooligomers. The protein is involved targetting LT-.alpha. to the cell surface. The LT-.alpha./LT-.beta. complex may act as an inflammation regulating agent, a tumor growth inhibiting agent, a T cell inhibiting agent, a T cell activating agent, an **autoimmune disease** regulating agent, or an HIV inhibiting agent (no data). Furthermore, the antitumor activity of the LT-.alpha./LT-.beta. complex may be delivered to tumor cells by tumor infiltrating lymphocytes (TILs) transfected with the gene for LT-.beta. (no data). LT-.beta. was identified as the protein

with which LT-.alpha. was bound on the surface of T-cells. The protein was only found in B- and T-cells. Cloning of a cDNA for LT-.beta. by PCR using amino acid sequence-derived primers is described; the cDNA was expressed using the pCDM8 expression cassette with successful expression achieved even without the initiator AUG codon.

L32 ANSWER 8 OF 8 MEDLINE DUPLICATE 1
93208881 Document Number: 93208881. PubMed ID: 7916655. Lymphotoxin beta, a novel member of the TNF family that forms a heteromeric complex with lymphotoxin on the cell surface. Browning J L; Ngam-ek A; Lawton P; DeMarinis J; Tizard R; Chow E P; Hession C; O'Brine-Greco B; Foley S F; **Ware C F**. (Biogen Incorporated 14 Cambridge Center, Massachusetts 02142.) CELL, (1993 Mar 26) 72 (6) 847-56. Journal code: CQ4; 0413066. ISSN: 0092-8674. Pub. country: United States. Language: English.
AB The lymphokine tumor necrosis factor (TNF) has a well-defined role as an inducer of inflammatory responses; however, the function of the structurally related molecule lymphotoxin (LT alpha) is unknown. LT alpha is present on the surface of activated T, B, and LAK cells as a complex with a 33 kd glycoprotein, and cloning of the cDNA encoding the associated protein, called lymphotoxin beta (LT beta), revealed it to be a type II membrane protein with significant homology to TNF, LT alpha, and the ligand for the CD40 receptor. The gene for LT beta was found next to the TNF-LT locus in the major histocompatibility complex (MHC), a region of the MHC with possible linkage to **autoimmune disease**.
These observations raise the possibility that a surface LT alpha-LT beta complex may have a specific role in immune regulation distinct from the functions ascribed to TNF.

=> s l27 and insulin dependent diabetes mellitus
L33 0 L27 AND INSULIN DEPENDENT DIABETES MELLITUS

=> s l27 and multiple sclerosis
L34 1 L27 AND MULTIPLE SCLEROSIS

=> d l34 cbib abs

L34 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
2001:781125 Document No. 135:343309 Ligand p30/LIGHT for HVEM (herpes virus entry mediator) and methods of therapeutic use. **Ware, Carl F.** (La Jolla Institute for Allergy and Immunology, USA). PCT Int. Appl. WO 2001079496 A2 20011025, 104 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US11857 20010411. PRIORITY: US 2000-524325 20000313; US 2000-549096 20000412.
AB A novel polypeptide ligand, p30, for HVEM (herpes virus entry mediator) and functional variations and fragments thereof are provided. The HVEM ligand is isolated from II-23.D7 cell line, a human CD4+ T cell hybridoma. P30, which can be found as a membrane protein and can function as a cytokine, is also called LIGHT, because this polypeptide is homologous to Lymphotoxins, exhibits Inducible expression, and competes with HSV Glycoprotein D for HVEM, a receptor expressed by T lymphocytes. Because LIGHT can compete with HSV glycoprotein D for HVEM, homo-trimeric sol. forms of this polypeptide can be used to block the entry of herpesvirus into cells. P30 is useful for modulating immune responses and in inhibiting infection and/or subsequent proliferation by herpesvirus. LIGHT also bind to the lymphotoxin-.beta. receptor (LT.beta.R). The present invention is also based upon the discovery that HVEM polypeptides

have an antagonistic effect on inflammation. In particular, HVEM fusion proteins are capable of inhibiting inflammation when administered to a subject. HVEM-Fc fusion proteins are also provided. Methods for treating subjects with lymphoid cell disorders, tumors, autoimmune diseases, inflammatory disorders of those having or suspected of having a herpes virus infection, utilizing p30 and the fusion proteins of the invention, are also provided.

=> s l27 and systemic lupus erythematous
L35 0 L27 AND SYSTEMIC LUPUS ERYTHEMATOUS

=> s l27 and myasthenia gravis
L36 1 L27 AND MYASTHENIA GRAVIS

=> d l36 cbib abs

L36 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
2001:781125 Document No. 135:343309 Ligand p30/LIGHT for HVEM (herpes virus entry mediator) and methods of therapeutic use. **Ware, Carl F.** (La Jolla Institute for Allergy and Immunology, USA). PCT Int. Appl. WO 2001079496 A2 20011025, 104 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US11857 20010411. PRIORITY: US 2000-524325 20000313; US 2000-549096 20000412.

AB A novel polypeptide ligand, p30, for HVEM (herpes virus entry mediator) and functional variations and fragments thereof are provided. The HVEM ligand is isolated from II-23.D7 cell line, a human CD4+ T cell hybridoma. P30, which can be found as a membrane protein and can function as a cytokine, is also called LIGHT, because this polypeptide is homologous to Lymphotoxins, exhibits Inducible expression, and competes with HSV Glycoprotein D for HVEM, a receptor expressed by T lymphocytes. Because LIGHT can compete with HSV glycoprotein D for HVEM, homo-trimeric sol. forms of this polypeptide can be used to block the entry of herpesvirus into cells. P30 is useful for modulating immune responses and in inhibiting infection and/or subsequent proliferation by herpesvirus. LIGHT also bind to the lymphotoxin-.beta. receptor (LT.beta.R). The present invention is also based upon the discovery that HVEM polypeptides have an antagonistic effect on inflammation. In particular, HVEM fusion proteins are capable of inhibiting inflammation when administered to a subject. HVEM-Fc fusion proteins are also provided. Methods for treating subjects with lymphoid cell disorders, tumors, autoimmune diseases, inflammatory disorders of those having or suspected of having a herpes virus infection, utilizing p30 and the fusion proteins of the invention, are also provided.

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---Logging off of STN---

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Executing the logoff script...

=> LOG Y